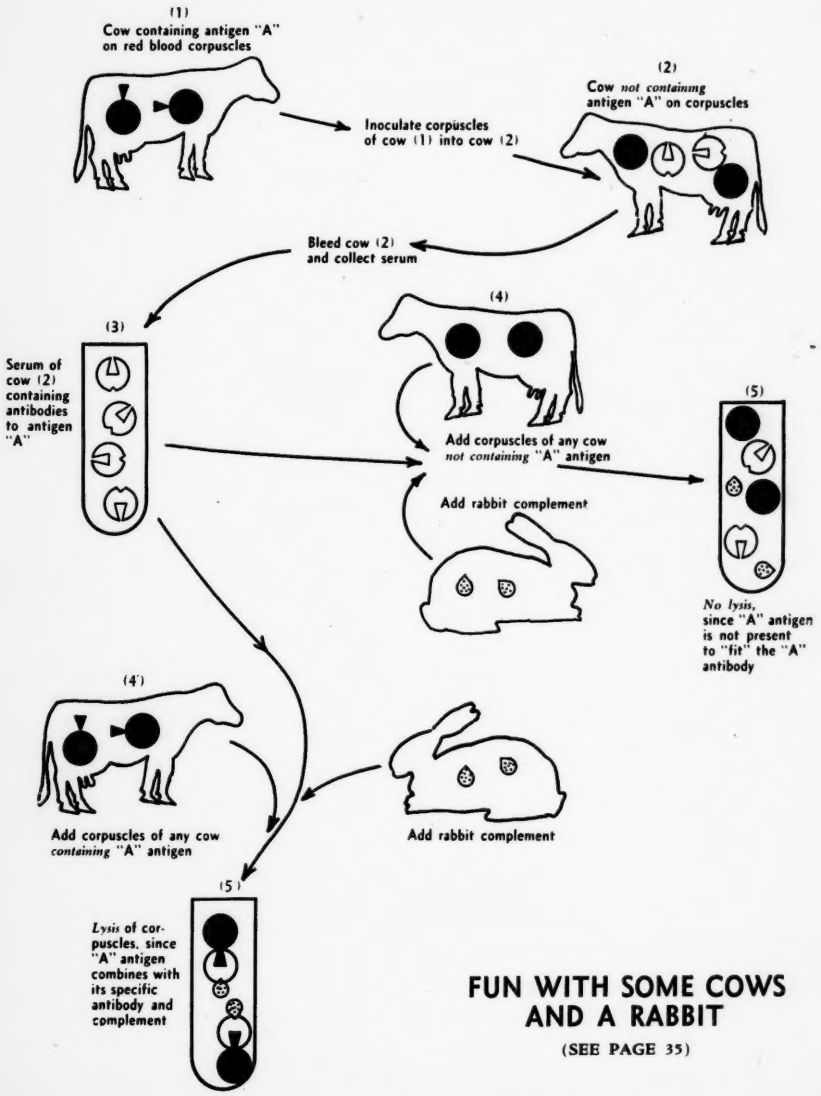
The Journal of HEREDITY


(1)
Cow containing antigen "A" on red blood corpuscles
(2)
Cow *not containing* antigen "A" on corpuscles
Inoculate corpuscles of cow (1) into cow (2)
Bleed cow (2) and collect serum
(3)
Serum of cow (2) containing antibodies to antigen "A"
(4)
Add corpuscles of any cow *not containing* "A" antigen
Add rabbit complement
(5)
No lysis, since "A" antigen is not present to "fit" the "A" antibody
(4')
Add corpuscles of any cow *containing* "A" antigen
Add rabbit complement
(5')
Lysis of corpuscles, since "A" antigen combines with its specific antibody and complement

FUN WITH SOME COWS AND A RABBIT

(SEE PAGE 35)

VOLUME 34 FEBRUARY, 1943 NUMBER 2

The American Genetic Association

An incorporated organization devoted to promoting a knowledge of the laws of heredity and their application to the improvement of plants, animals, and human racial stocks

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The

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Antigens in blood cells =
A C E G I Q W X Z E' H'

Blakeford Prince George 262190
Antigens in blood cells =
A B C E G H K S W Y Z A' C' G' H'

Guernsey Calf: U. W. Merry
Antigens in blood cells = *A C E H I O Q R S W Z E' H'*

WHICH BULL IS *NOT* THE SIRE OF U. W. MERRY?

Figure 1

Thirty distinct red blood cell antigens have been discovered in cattle. These are inherited independently and according to a simple Mendelian pattern. Whenever one of these antigens is present in the blood of an animal, it has been shown to be present universally in one or both of the parents. In practice it has been found possible to differentiate every cow from every other cow (except identical twins) by these antigens. These photographs illustrate a practical use of this technique in instances wherein two possible bulls might be the sire of a given calf. In this case the antigen test proves that one of the bulls could not have been the sire of the calf U. W. Merry, on account of dissimilarities. The calf differs from its mother in the three antigens *H, O, R* and *S*. Two of the antigens could only have been inherited from one of the putative sires. Hence the other is excluded as a possible parent. See page 39 for details. Photographs furnished by G. R. Barrett and C. E. Zehner, Department of Dairy Husbandry, University of Wisconsin.

parent. See page 39 for details. Photographs furnished by G. K. Barrett and C. E. Zeimer, Department of Dairy Husbandry, University of Wisconsin.

CELLULAR ANTIGENS IN CATTLE BLOOD*

CLYDE STORMONT AND R. W. CUMLEY
University of Wisconsin

EARLY in the studies designed to throw light upon the complex problems of immunity, Ehrlich and Morgenroth[1] postulated that in its chemical structure the red blood cell must have a large number of side-chains with different chemical groupings to account for the diverse reactivities determined by immunological tests. Subsequent studies have shown that intact cells contain a number of antigens which differ in their specific immunologic properties and accordingly lend themselves to differentiation by the proper immunological procedures. Reports[2,3] from this laboratory have revealed that at least 30 different antigenic characters may be recognized in the red blood cells of cattle. These antigens appear to be inherited as independent characters and the typing of any individual for the presence or absence of these antigenic characters has served to differentiate every animal from every other, except in the case of identical twins.

The following presentation shows diagrammatically the steps necessary for the identification of antigenic characters in cattle blood.†

Explanation of Figure 2

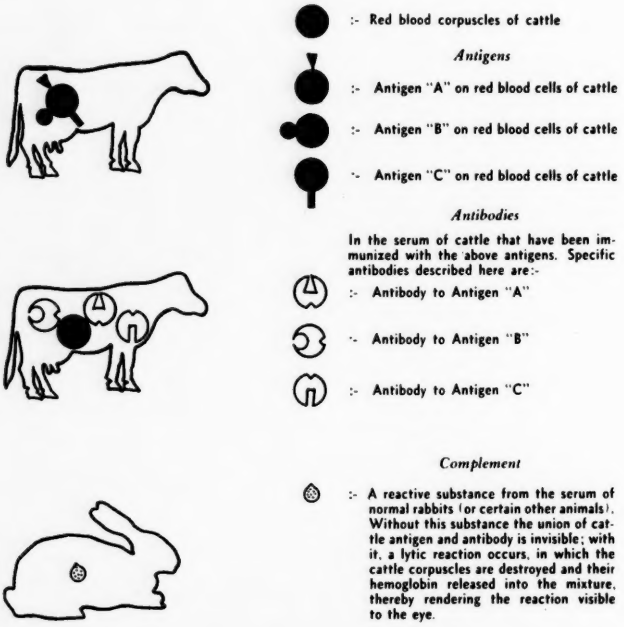
In Figure 2 the red blood cell of cattle is shown as a solid black disk, and the antigens, represented as *A*, *B*, and *C* are depicted on the surface or stroma of the cell. The presumption is that when any or all of these antigens on the intact cells are injected into an organism not possessing them, highly specific antibodies will be produced against each of the respective antigens introduced. Thus, in Figure 2, if the red blood cells of the cow possessing the three antigens *A*, *B*, and *C* are inoculated into the second cow whose red blood cells contain none of these three antigens, the production of an immune serum‡ containing the three highly specific antibodies to antigens *A*, *B*, and *C* would be expected. It is important to note that the antibodies supposedly are as qualitatively distinct as are the antigens they define; i.e., the antibody to *A* is depicted as fitting only *A* antigen and hence capable of reacting only with *A* antigen, etc. When this immune serum is tested, while fresh, with the corpuscles of individual animals having antigens *A* or *B* or *C* or any combination of these three, the corpuscles are agglutinated into clumps plainly visible to the eye.

If the fresh immune serum is heated for an hour at 56° C., or is aged for several days, it loses its ability to agglutinate the cells having the specific antigens. This loss in activity is not due to disappearance of the respective antibodies, but to the loss of a third component necessary in bringing out the reaction that actually does take place between antigen and antibody. This third component is a heat-labile, non-specific substance known as "complement." Complement is usually present in the fresh unheated serum of normal animals. Therefore the ability of this heated serum to agglutinate cells is restored by the addition of fresh normal beef serum. A more sensitive test may be made by adding fresh normal rabbit serum to reactivate the (heated) immune serum. When this immune serum is mixed with cells having the respective antigens in the presence of rabbit complement the

*Paper No. 307 from Departments of Genetics and Veterinary Science, Agricultural Experiment Station, University of Wisconsin. The authors wish to express their appreciation of the helpful criticism offered by Dr. M. R. Irwin in the preparation of the manuscript.

†See bibliography (4 and 5) for two similar presentations showing the antigenic differences between two dove species and the interaction of antigens in dove hybrids.

‡Such an immune serum is called an isoimmune serum; i.e., one produced by immunizing with the cells of the same species.


:- Red blood corpuscles of cattle
Antigens
:- Antigen "A" on red blood cells of cattle
:- Antigen "B" on red blood cells of cattle
:- Antigen "C" on red blood cells of cattle
Antibodies
In the serum of cattle that have been immunized with the above antigens. Specific antibodies described here are:-
:- Antibody to Antigen "A"
:- Antibody to Antigen "B"
:- Antibody to Antigen "C"
Complement
:- A reactive substance from the serum of normal rabbits (or certain other animals). Without this substance the union of cattle antigen and antibody is invisible; with it, a lytic reaction occurs, in which the cattle corpuscles are destroyed and their hemoglobin released into the mixture, thereby rendering the reaction visible to the eye.

ANTIGENS AND ANTIBODIES IN CATTLE

Figure 2

The relations of antigens, antibodies, and complement are diagrammed in this chart and explained in detail on page 35. The reaction between the antigens, antibodies, and complement which produce hemolysis are entirely specific; each antigen combines only with a specific antibody. Since thirty antigens have been demonstrated in cattle, it is obvious that the outline shown here is an extreme simplification.

cells are hemolysed. Hemolysis of the red blood cells is easily observed *in vitro* because of the free hemoglobin pigment liberated from the cells. The rabbit complement alone has no action on the red blood cells and mediates its effect only through the specific antibodies. Complement from guinea pigs is not as usable in these tests, since antibodies for cattle cells are found in the normal serum of many guinea pigs. Complement combines with antibodies only when the latter are adsorbed on the cells by virtue of union with their specific antigens. In Figure 2 the complement molecule is so depicted that it fits into the wedge on the antibodies. Thus the three essential components for a hemolytic test of the red blood cells of cattle are antigens, their specific antibodies, and complement.

A test on the corpuscles of one individual requires only two drops of this immune serum, diluted according to its titer, usually 1:8, one drop of a 3 per cent suspension of washed red blood cells, and one drop of complement (fresh, undiluted rabbit serum).

If we were to use the hypothetical immune serum as proposed above in tests on the corpuscles of various cattle, it is apparent that it would be almost impossible to know, in cases of a positive reaction, whether the cells of any one individual were reacting because of all three antigens, to a combination of any

two, or to any one alone. In other words, a testing fluid containing antibodies for only one antigen, as *A*, is required before we can definitely state which of these cellular components is present in the corpuscles of any animal. Such testing fluids containing specific antibodies for only one character are designated as "reagents." Figure 3 illustrates a hypothetical case for the simplest known method of producing an immune serum containing specific antibodies for only one cellular character.

Explanation of Figure 3

(1) This cow is pictured as having only one antigen, *A*, not present on the corpuscles of the cow in (2). Since cow (2) does not have antigen *A*, inoculation of the corpuscles of cow (1) into cow (2) should result in the formation of specific antibodies against antigen *A* as shown.

(2) After several inoculations, usually over a period of three or four weeks, of the corpuscles of cow (1) into (2), antibodies for antigen *A* are produced in maximum potency. Trial samples of serum are taken from cow (2) before each immunization and at times between the inoculations to ascertain the titer of the antibodies produced.

(3) When the antibody titer of cow (2) appears to have reached a maximum, she is bled and the serum collected. Two liters of blood from cow (2) should yield approximately one liter of serum. If used in a routine dilution of 1:8, one liter of serum could be used to test the corpuscles of nearly 80,000 animals.

(4) When this immune serum is tested with the corpuscles of a cow not having antigen *A*, the corpuscles behave as if they were in an isotonic salt solution. After an hour or so, they settle to the bottom of the tube (5) and leave a clear supernatant fluid containing free antibody and complement.

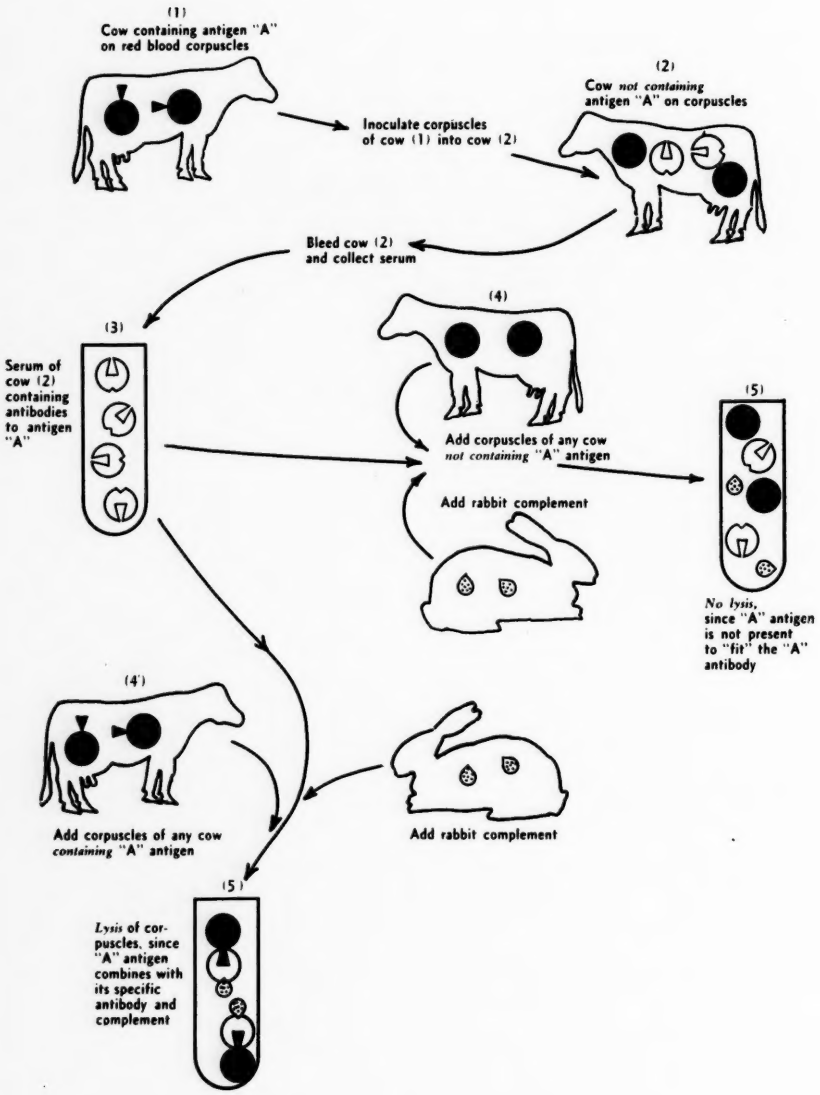
(4′) But when the immune serum is tested with the corpuscles of a cow having antigen *A*, hemolysis of the red blood cells ensues (5′) leaving nothing but a clear red fluid plainly visible to the eye. If the hemolysis is incomplete, as would occur with high dilutions of either the reagent or complement, the reaction is still markedly noticeable.

The diagram shows that the immune serum from cow (2) contains an antibody for but one cellular substance, antigen *A*. The validity of this assumption may be tested by absorbing the antiserum with any reactive cells. The reactive cells of any individual should remove by absorption the antibody—and therefore this fluid would not lyse previously reactive cells—while absorption by non-reactive cells should not materially affect the antibodies of the antiserum. The conclusion from such tests would be that the antibodies reacted with but a single antigen. Were antibodies present for more than one cellular substance, it would be anticipated that different combinations of these substances would be found in different individuals. Further evidence that this reagent reacts with only one antigen is obtained by comparing the segregation of antigen *A* in the progeny of matings in which one or both parents carry *A*, and testing the results with those expected by the gene frequency method.

In actual practice, few isoimmune sera would be expected to be as simple as the example in Figure 3, since the 30 known antigens in cattle give rise to a large number of diverse combinations. The several steps necessary in the preparation of unit reagents from a more complex isoimmune serum are shown diagrammatically in Figure 4.

Explanation of Figure 4

(1) and (2) The red blood cells of cow (1) are shown to have two antigens, *B* and *C*, not present on the corpuscles of the cow in (2). Both cows are depicted to have antigen *A* in common; actually they may have many more in common, and cow (2) may have several cellular components not found in the corpuscles of cow (1). The important factor to consider in the inoculation of cow (2) with the corpuscles of


(1)
Cow containing antigen "A" on red blood corpuscles
(2)
Cow *not containing* antigen "A" on corpuscles
Inoculate corpuscles of cow (1) into cow (2)
Bleed cow (2) and collect serum
(3)
Serum of cow (2) containing antibodies to antigen "A"
(4)
Add corpuscles of any cow *not containing* "A" antigen
Add rabbit complement
(5)
No lysis, since "A" antigen is not present to "fit" the "A" antibody
(4')
Add corpuscles of any cow *containing* "A" antigen
Add rabbit complement
(5')
Lysis of corpuscles, since "A" antigen combines with its specific antibody and complement

PRODUCTION OF ANTIBODIES

Figure 3

The production of *A* antibodies in a "non-*A*" cow is diagrammed with an outline of how this antigen is demonstrated. See page 37 for details.

cow (1), is that the latter has two antigens, *B* and *C* which should engender the production of specific antibodies to both antigens as shown in steps (2) and (3). Cow (2) will not produce antibodies to antigen *A* or any other antigen which she shares with cow (1).

(4) and (5) Since certain cattle have antigen *C* but not antigen *B* on their corpuscles, and vice versa, a practical method is available for the separation of antibodies for *B* and *C* antigens. If a sample of the immune serum of cow (2) is mixed with the corpuscles of a cow having character *C*, the antibodies for *C* will be adsorbed onto the corpuscles, leaving the antibodies for antigen *B* free in the supernatant fluid that separates from the cells following centrifugation.

(6) and (7) The resulting decanted serum is now a unit reagent, since it supposedly contains antibodies for antigen *B* only. When this reagent is tested with corpuscles of individuals having antigen *B*, a positive hemolytic reaction (7) occurs.

The preparation of a testing fluid for the *C* antigen would follow a parallel procedure, except that the red blood cells of an animal having antigen *B* and not *C* would be used in the absorption process.

Absorptions and gene frequency analyses may be carried out on either of these reagents in the manner described earlier for antigen *A*, to show that these two reagents react with only one antigen, respectively.

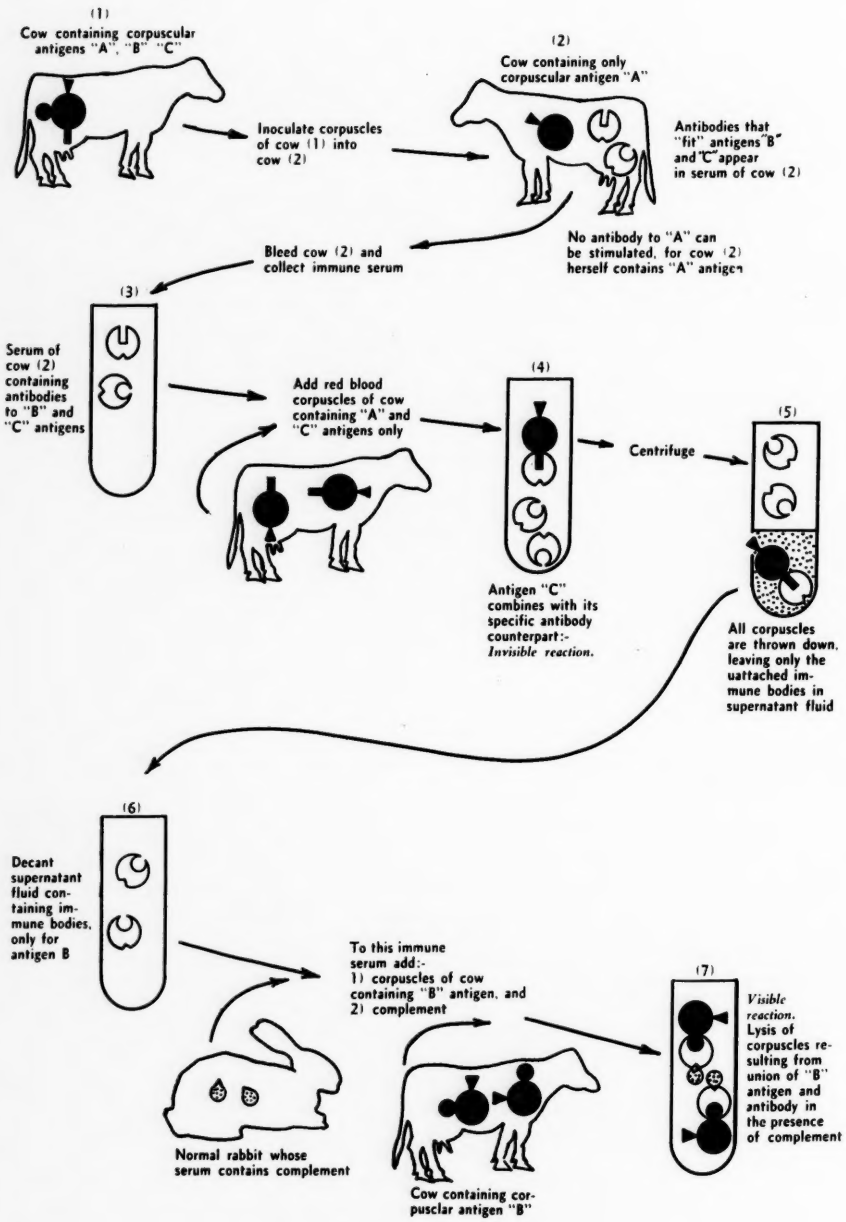
The absorbed reagents for the identification of antigens *B* and *C* respectively, in conjunction with the immune serum for antigen *A*, may now be used for the identification of antigens *A*, *B*, and *C* in the erythrocytes of cattle. Eight phenotypes may be detected by these three reagents—*ABC*, *AB-*, *A-C*, *-BC*, *A—*, *—B—*, *—C*, and —, the dash indicating the absence of one or more antigenic characters.

Explanation of Figure 5

Figure 5 illustrates the inheritance of antigens *A*, *B*, and *C* in the offspring of a bull, having all three antigens, mated to a cow having only antigen *A*. If the bull is heterozygous for these three antigens and the dam is homozygous for antigen *A* and lacks characters *B* and *C*, there are four types of offspring possible, and they are represented in the figure. Since the heterozygotes cannot be distinguished from the homozygotes in these tests, the only way to determine the genotype is the analysis of the blood characters of a considerable number of offspring from any one individual.

Explanation of Figure 1

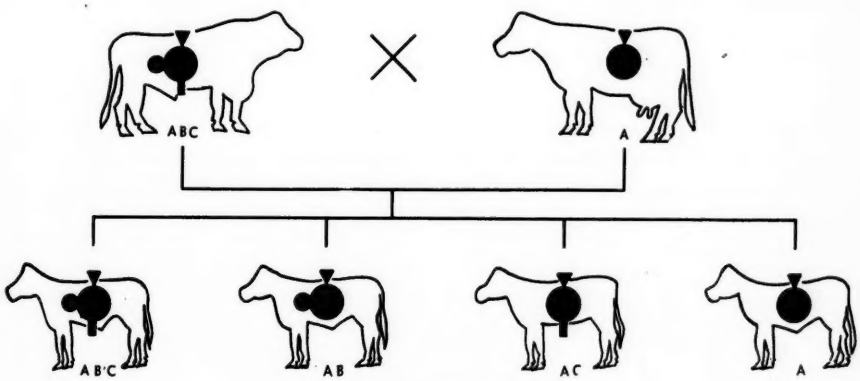
Figure 1 illustrates a practical application of the cattle blood tests, using reagents which identify thirty different red blood cell antigens in cattle. Actual tests have shown that whenever one of the known antigens is present in the blood of an animal, it was also present in the blood of one or the other or both parents. The case presented here shows one of the most common problems arising in disputed parentage: Which of the two bulls is the correct sire of the Guernsey calf, U. W. Merry? If the dam had been mated to both of these two bulls at the same period of heat, it would be impossible to exclude one of these bulls as the sire of the calf on the basis of any other known tests. The blood tests show, in this case, that Blakeford Prince George 262190 is readily excluded as the sire of the calf, U. W. Merry. The exclusion of this sire is made possible by comparing the antigens of the calf's blood with those of her dam, and of the two bulls. The calf has the characters *H*, *O*, *R*, and *S* which are not present in her dam's blood; therefore these antigens must be inherited from her sire. MacDonald Farm's Beau Brummel 249620 has all four of these cellular components, whereas Blakeford Prince George is excluded as the true sire of U. W. Merry on the basis of his lacking antigenic characters *O* and *R*. Hence MacDonald Farm's Beau Brummel may very well be the true sire of U. W. Merry. It cannot be asserted positively that Beau Brummel


(1)
Cow containing corpuscular antigens "A", "B" "C"
Inoculate corpuscles of cow (1) into cow (2)
(2)
Cow containing only corpuscular antigen "A"
Antibodies that "fit" antigens "B" and "C" appear in serum of cow (2)
No antibody to "A" can be stimulated, for cow (2) herself contains "A" antigen
Bleed cow (2) and collect immune serum
(3)
Serum of cow (2) containing antibodies to "B" and "C" antigens
Add red blood corpuscles of cow containing "A" and "C" antigens only
(4)
Antigen "C" combines with its specific antibody counterpart:- *Invisible reaction.*
Centrifuge
(5)
All corpuscles are thrown down, leaving only the uattached immune bodies in supernatant fluid
(6)
Decant supernatant fluid containing immune bodies, only for antigen B
To this immune serum add:- 1) corpuscles of cow containing "B" antigen, and 2) complement
Normal rabbit whose serum contains complement
Cow containing corpusclar antigen "B"
(7)
Visible reaction. Lysis of corpuscles resulting from union of "B" antigen and antibody in the presence of complement

PRODUCTION OF A *B* REAGENT

Figure 4

The production of *B* and *C* antibodies in a cow is shown with a demonstration of how the two antibodies are separated by differential absorption. See page 39 for details.



INHERITANCE OF ANTIGENS

Figure 5

Chart showing the segregation of three antigens in the blood corpuscles of cattle. Antigen *A* is represented as contained in both parents. Antigens *B* and *C* are present only in one parent. The four possible types of offspring from this cross are shown in the lower line. If an antigen appears in an offspring, it must be present in one or both parents. For further details see page 39.

is the sire,—only that he *could be* the sire. *Parentage* cannot be proved by virtue of the blood tests, only *non-parentage*. If only two bulls have served the cow, one might be excluded as the sire of the calf; the other, then, could be assumed to be the correct sire.

Once the blood of an animal has been typed, it can be distinguished from almost all others because of the large number of possible combinations of the blood characters. Recently, three Holstein heifers, in a herd of thirty-five experimental animals at this University, lost their ear tags. The herdsman could not identify them. All thirty-five heifers had been typed the previous month. Duplicate blood tests from these three animals served readily to identify them according to their previous numbers.

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TEMPERATURE AS A FACTOR IN EVOLUTION

LIKE volumes II and IV of the *Biological Symposia,* this sixth member of the series* is chiefly concerned with some aspects of evolutionary biology. The papers composing the new volume were presented at three symposia held at the Dallas 1941-42 meeting of the American Association for the Advancement of Science under the titles: "Temperature and Evolution," "Isolating Mechanisms" and "Genetic Control of Embryonic Development." In his foreword to this volume, Prof. Th. Dobzhansky thus pictures the role of scientific symposia:

> Theories, speculations and techniques are like assorted keys which we are trying to fit to the locks of unsolved problems. It is best if the fitting trials are made by those who wield the tools of active investigators. For the accidentally found keys almost never completely fit the locks, and some finishing touches on the keys are necessary before a satisfactory fit is at last obtained. Moreover, it is obviously important to distinguish bona fide keys from spurious ones. Scientific symposia are, or should be, organized cooperative attempts to find keys that open the known locks, and to identify the locks the keys to which must be found in the future.

The reservation contained in the words "are, or should be" is fully justified by the first symposium on "Temperature and Evolution." It is not quite clear which is the lock that it is proposed to open at this symposium. In other words, the reviewer does not think that the subject of the symposium was a fortunate choice. The links of most of the papers with either temperature or evolution are artificial or loose, and the whole forms a rather heterogeneous structure, presenting no unity of purpose.

The symposium includes papers by eight authors. H. H. Plough presents evidence that spontaneous gene mutations are more frequent at higher temperatures and suggests that "it is perhaps this relation of temperature to mutation which determines the greater number of species in tropical areas." G. Fankhauser shows that very low temperature treatments frequently induce polyploidy in the laboratory and that similar changes might occur from time to time in nature. However, "the role played by polyploidy in the evolution of animals remains to be clarified." G. P. Child presents data which seem to indicate a greater stability, with respect to temperature changes, of the phenotypic characteristics of wild type as compared with those of mutant types. "This peculiarity of wild type developmental processes may be a result of natural selection which in general favors a genotype which produces relatively uniform phenotype." E. Witschi discusses the origin of the so-called differentiated and undifferentiated sex races of the European frog, *Rana temporaria.* The differentiated races are "hereditarily fixed variations of exactly the same morphological type as the environmental (phenotypical) modifications which appear in undifferentiated races if transferred under identical climatic conditions" (among the latter, temperature is the only one that shows a clear correlation with the sex-type of the local races). Concerning the evolutionary origin of these races, Witschi holds a very unorthodox view: he rejects selection of chance variations (mutations) and favors directed genetic changes induced by temperature conditions via ovarial and testicular substances. H. J. Muller presents a penetrating analysis of the whole problem of the establishment of genetically determined isolation. Having discussed the various mechanisms which can be conceived to bring about such isolation, Muller shows how temperature may affect these various processes. It appears that in some respects the warmer regions of the globe would favor a greater evolutionary diversity, while the colder regions would provide evolutionary

**Biological Symposia,* Volume VI. Temperature and Evolution. Isolating Mechanisms Genetic Control of Embryonic Development. Pp. XII + 355. The Jaques Cattell Press, Lancaster, Pa., 1942.

stimuli, particularly to the more advanced forms. W. Landauer shows how the manifold effects of the mutant "Frizzle" in the domestic fowl may be traced back to an increased loss of body heat, due to plumage defects. Many of the phenotypic changes are in the nature of partial adaptations or compensations to the excessive loss of heat. The probable existence of mutational changes affecting the extent of functional adaptability is particularly interesting from the evolutionary point of view. A. C. Kinsey presents a study of clines in emergence dates in the gall wasps. In some cases there appears to be a correlation with temperature conditions, but in other cases emergence is in late winter in the northernmost part of the cline and in late spring in the southernmost. "The continuation of the north-south clines beyond the point where there is any correlation with lowering winter temperatures . . . . suggests some sort of momentum, an orthogenesis or some other linear development that proceeds without apparent adaptation to or selection by particular factors." However, the author recognizes that "in the present state of our knowledge of genetics, it would be rash to accept an orthogenetic explanation of clines." J. H. Moore discusses the distribution of species of frogs in Eastern North America in relation to their temperature tolerance. A close correlation is found between the northern limit of range and the range of temperature tolerance. Differences in size of eggs, rate of development and other characters are also found to be correlated in the same way.

In contrast to this first set of papers, the second symposium forms a consistent and homogeneous unit, sharply aimed at a well-defined problem, the "Isolating Mechanisms."

The only botanist participating in the symposium, G. L. Stebbins discusses isolating mechanisms in plants with emphasis on genetically determined hybrid sterility and on the relationship between isolating mechanisms and morphological divergence (the "descent with modification" of Darwin). There appears to be "no direct correlation between the genetic changes which make species visibly different." A. P. Blair analyses isolating mechanisms in toads. Ecological, seasonal and sexual isolation are the predominant mechanisms, hybrid sterility playing little if any role. A. C. Kinsey, in the outstanding article of this series presents taxonomic data on "isolation as a process in the speciation of gall wasps of the family *Cynipidae*." Species and lower categories are shown to be isolated primarily geographically. In higher categories isolation through use of different hosts and "cytologic" isolation (hybrid sterility) become of increasing importance. "Although the genera and tribes are undoubtedly isolated now by cytologic mechanisms, their peculiar host restrictions suggest that the choice of host, a product of the insect's physiologic reactions, was the original basis for differentiation of these major groups." Speaking for the active Austin group, J. T. Patterson presents the results of extensive investigations of the isolating mechanisms in several groups of Drosophila species. At least six different types of isolating mechanisms are encountered in various combinations and appear to have different importance in different groups. The genetic analysis reveals different modalities of gene-control in the establishment of the various isolating mechanisms.

In the early phases of growth of a new discipline like developmental genetics, the theme of the third symposium, a clear definition of what Prof. Dobzhansky calls in the foreword, its "right course," is of undoubted importance! "Our attention should be concentrated primarily on those problems which are capable of solution with the aid of methods now available. But we must not lose sight of the problems which are as yet unsolvable, since one cannot consciously seek the means of approach to problems the existence of which is forgotten." V. C. Twitty, in an article whose title ("The role of genetic differentials in the embryonic development of Amphibia") does not reflect its content, and whose content depicts an attitude

of discouraging doubt rather than of stimulating conviction, sets out to determine the "right course" in the integrated field of embryology and genetics. Twitty, to use again Prof. Dobzhansky's terms, has certainly not lost sight "of the problems which are as yet unsolvable"; unfortunately, he has not "concentrated primarily on these problems which are capable of solution with the aid of methods now available." Of the twenty pages of his article hardly a third contains condensed accounts of his own excellent experimental work on the differences in pigment pattern between species of salamanders. The rest of the paper is a confused argument (or should one rather say "complaint"?) about the (sometimes very real) difficulties of integrating genes and development. The argument is methodologically weak and self-destroying by the accumulation of contradictions. The reviewer can, however, agree with the author when, obviously aware of the weakness of his argumentation, he writes at the end of his paper: "In concluding what may appear to be a pessimistic harangue, it is as well to confess, before someone points it out, that I have been guilty to some extent of 'setting up straw men'." As a compromise imposed by the present-day posibilities, the reviewer will also agree that "after all, more important than whether genetics and embryology become blended into one, is the extent to which each field stimulates and facilitates productive activity in the other" and he definitely believes that "this is the true measure of the progress which is being made, and is reflected, for example, in such investigations as those of the other participants in this symposium." The two other papers of the symposium indeed form a striking contrast with that of Twitty. V. Hamburger presents a careful embryological analysis of the multiple effects of the creeper factor in the chick. The various symptoms are found to be produced via at least four different channels: yolk sac circulation, chondrogenesis, head mesoderm, growth; but the four main effects cannot be reduced to one basic gene action as yet. This, in the author's opinion, must await the intervention of physiological and biochemical methods of analysis. "The complete story of the mode of gene action must be written jointly by geneticists, embryologists and physiologists." In the last paper of the volume, S. Wright gives a new account of his extensive work on the relations between the principal color factors of the guinea pig. The relatively simple "processes and patterns of the pigment system seem to give a model case which is favorable for obtaining an insight into the chains of events connecting the system of genes with developmental patterns." The concluding pages of the paper contain a lucid and inspiring discussion of the general problem of heredity in relation to development.

As in all symposia, the majority of papers, due to their review-nature, bring no real novelty, but the volume as a whole is extremely valuable in giving the reader a clear picture of the status and the movement of ideas in two of the youngest and most active branches of modern genetics.

Boris Ephrussi

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POLYDACTYLISM IN RELATED NEW ENGLAND FAMILIES

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THOUGH polydactylism is by no means uncommon in man it has attracted attention and comment from early times. It is mentioned in the Second Book of Samuel, ch. 21, v. 20: "And there was yet a battle in Gath, where was a man of great stature, that had on every hand six fingers and on every foot six toes, four and twenty in number; and he also was born to the giant." Pliny[10] knew of it, for he wrote: "Some men there be, with six fingers to one hand. We have heard, that M. Curiatius, a nobleman of Rome, had two daughters so handed: whereupon they were surnamed Sedigitae. Also there was a man named Volcatius, who was an excellent Poet, and had six fingers to an hand, whereupon he was surnamed Sedigitus."

The cases described in more recent literature are drawn from many different nationalities and racial stocks. From this it seems probable that this modification has appeared independently at widely separated times and places and in unrelated individuals. Such a probability is also suggested by the occurrence of polydactylous individuals in families in which there is no known history of the character, though such cases should be regarded with skepticism and carefully investigated.

Most affected individuals have polydactylous relatives, and the hereditary nature of the condition has long been recognized. Studies of families in which the character appears have indicated that it usually depends on a single dominant factor. Frequently there is considerable irregularity in inheritance, and in some pedigrees the distribution of affected individuals seems to indicate that a recessive factor is responsible.

The term polydactylism is by no means specific. It implies the presence of extra digits, but the number of extra digits, the degree of their development and their position on the extremities may be markedly different in different pedigrees. It seems evident that different hereditary factors are responsible for these various types of polydactylism, and their type of inheritance may be expected to vary, as well as their effects.

In addition to the differences between unrelated pedigrees there is also considerable variation in the manifestation of the condition in a single pedigree. This seems to be the result of variability in the operation of the gene responsible, though it has been suggested that such variation may be the expression of changes in the organization of the gene.

In the pedigree presented here the polydactylous condition is characterized by the appearance of a single extra digit on the post-axial border of the hand or foot. The distribution is subject to considerable variation. Since there are four extremities, any or all of which may bear an extra digit, fifteen possible arrangements may be expected. Six of these are represented in the cases recorded, and it seems likely that others have occurred. There is also variation in the degree of development of the extra digit. It may closely resemble the adjacent (fifth) digit and articulate with a supernumerary metacarpal or metatarsal, or it may be a mere fleshy protuberance. Intermediate conditions also occur.

In the preparation of the pedigree charts conventions in common use have been employed, but the meaning of certain symbols must be explained. Each circle (♀) or square (♂) is considered to be divided into four quarters, each of which corresponds to one extremity. The upper quarters represent

the hands, the lower quarters the feet, while right and left correspond to the reader's right and left. A solid black symbol thus denotes a completely polydactylous individual; a symbol in which the lower half is black indicates an individual with extra toes but normal hands; and so on. In cases in which only one hand or foot is affected and the side of the body is not known the central portion of the appropriate half of the symbol is black. A symbol containing an X denotes an individual known merely to have been affected; one containing a question mark denotes lack of information. Empty symbols have two meanings: if a polydactylous individual has previously occurred in that line of descent, they denote normal or apparently normal persons; previous to the first appearance of a polydactylous individual they merely indicate lack of information. When a number is used in place of a symbol it denotes a corresponding number of normal individuals; if followed by an X, a corresponding number of polydactylous individuals. An X alone indicates an unknown number of affected descendants. In the early generations where information regarding polydactylism is lacking the families represented are by no means complete, though genealogical information concerning them is often available.

Individuals are referred to in the text by the numbers of the symbols by which they are indicated in the pedigree charts combined with the number of the generation of which they are a member. This is necessary because many of the records which have made this study possible were made available with the understanding that no names should be revealed. Some of the information was supplied by persons now living, with the same understanding. As a result many of the statements set off by quotation marks are not quotations in the strict sense, but care has been taken to preserve their meaning and as much of their wording as possible.

It has also been deemed necessary to omit references to published sources which contain statements that would reveal the identity of the families and individuals involved. It is nevertheless desirable that the information on which this study is based should be available for the use of other investigators. Accordingly, the genealogical material and references necessary to supplement this account will be deposited with the Genetics Record Office of the Carnegie Institution of Washington.

I am deeply indebted to those individuals who generously furnished information concerning their particular components of the pedigree. Had it not been for the interest of the man indicated as IXA-32 much of the pedigree of his branch of the family might have gone unrecorded, and its presentation here is due to the helpfulness of his sister-in-law, IXA-30, who transcribed these records and answered many questions concerning them.

Dr. A. F. Blakeslee, Director of the Department of Genetics of the Carnegie Institution of Washington, kindly permitted me to examine the files of the Genetics Record Office, and I am grateful for the assistance there of Dr. Barbara Burks. I am also indebted to Dr. Nathaniel W. Faxon, Director of the Massachusetts General Hospital, who supplied the hospital record which served as a beginning for the genealogical investigation of Family 3.

Family 1

(See Figure 6)

The information upon which this component of the pedigree is based was obtained from the polydactylous woman indicated as X-8. Her left hand and foot were affected, but the extra digits were poorly developed and were removed in infancy. One of her sons was completely polydactyl, the other normal. None of her sisters was affected. Her father and an uncle were unilaterally polydactyl. Another uncle who was affected transmitted the character to two of his children. One of these had extra toes while the other had extra toes and an extra finger on one hand. The woman's grandfather, VIII-12, like her affected son, was completely polydactyl.

During the investigation of the ancestry of these individuals the following statement was discovered: "IV-22 married III-24, his father's cousin. She had an unusual number of fingers and toes (a characteristic of the whole ——— family in America)." This couple is not among the ancestors of VIII-12, but his great-great-grandfather, IV-23, married IV-14. She was a niece of III-24 and may likewise have been polydactyl. In addition there is a possibility that IV-23 was himself affected, for his grandmother, II-5, was an aunt of III-24 and hence may also have been polydactyl.

Besides the three marriages between members of these families just mentioned, it is also to be noted that III-28 married his cousin, III-10. Either or both of these individuals may have been affected, but it is quite certain that one of them was, for it was subsequently learned that they had polydactylous descendants.

In this pedigree the polydactylous character is inherited as an ordinary dominant, though the manner of expression shows considerable variation. In four complete families having a polydactylous parent, seven out of 15 offspring are affected.

Upon the discovery that III-24 was polydactyl it was surmised that her father, II-1, who came to this country from England before 1644, and other members of his family were also affected. In one genealogy of the family the following statement is made: "A physical peculiarity has characterized the ——— family for many centuries—that is, an occasional excess in the number of the extremities, hands and feet, an extra finger or an extra toe. An old English medical book says that from 'as long as the 14th century this mark has been traced, sometimes almost disappearing, and then coming forth again in full vigor'." Another genealogy says: "As early as the fourteenth century, it was noted for its family mark, i.e., the extra finger and toe, not a very desirable distinction but one that is still conferred on some of its members." These genealogies give no information concerning specific cases, and it accordingly became necessary to search for pedigrees which gave promise of being related to this family. Those which follow have fulfilled this promise.

Family 2

The information on which this portion of the pedigree is based appeared in a genealogy, but was first seen in the files of the Genetics Record Office. The significant statement, with names replaced by the numbers by which these individuals are indicated in the charts, is as follows:

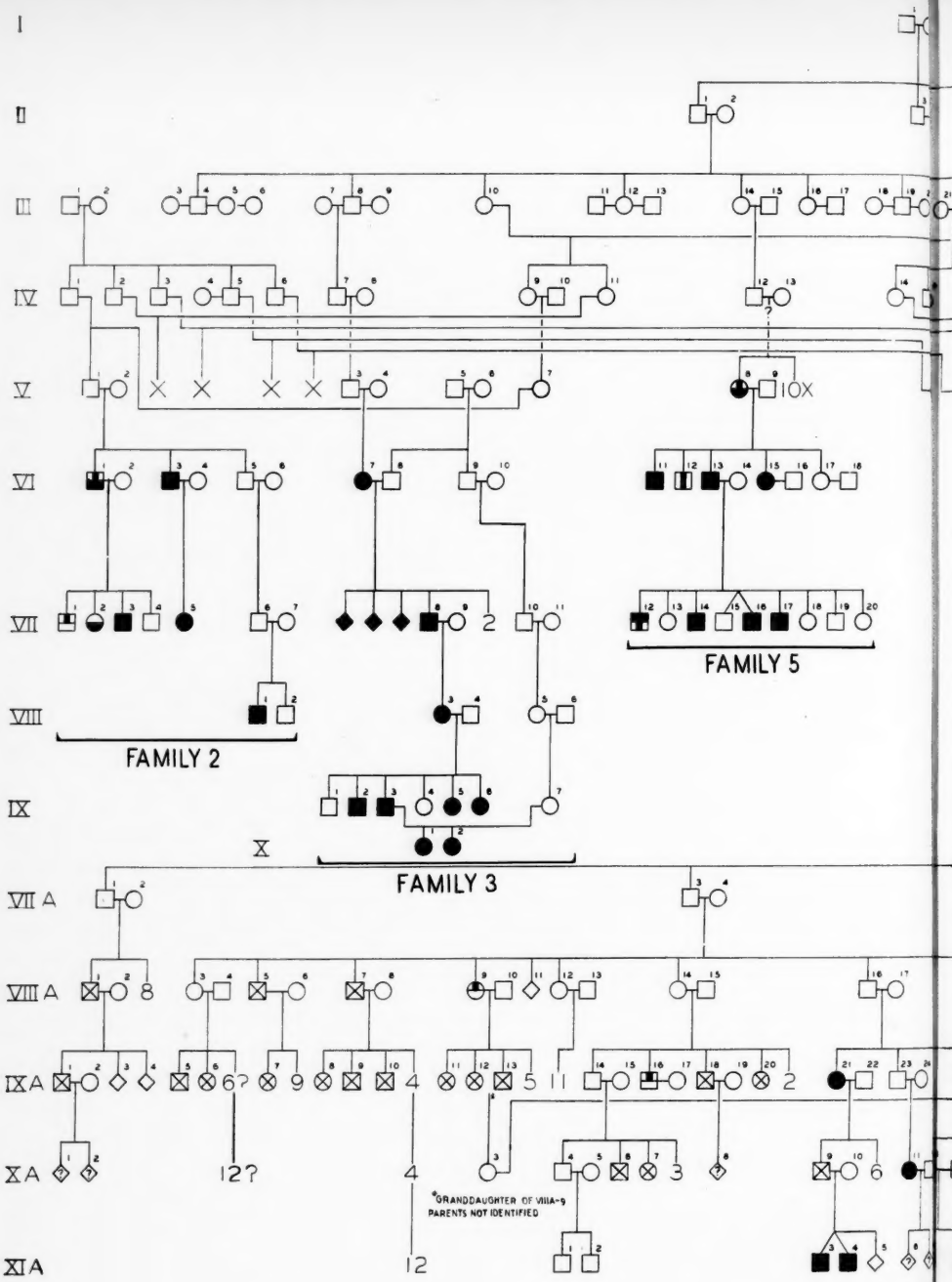
> VII-4, in a letter in 1880, stated that his father (VI-1) had six toes on each foot and five fingers on one hand and four on the other. One of the sons (VII-1) of VI-1 had five toes on each foot, five fingers on one hand and four on the other; one of his daughters (VII-2) had six toes on each foot and four fingers on each hand; another son (VII-3) had six toes on each foot and five fingers on each hand. Another son (VI-3) of V-1 and a daughter (VII-5) of that son had the same birthmark. A son of VII-6 had the same mark. Descendants of IV-2, who intermarried with Family 1, have the same distinguishing character, as well as (descendants of) other children (IV-3, 5 and 6) of III-1 who intermarried with the ——— family.

The only complete family of a polydactylous parent in this pedigree is that of which VII-4 is a member. He had three brothers and three sisters who are not represented in the chart and who, like himself, were presumably normal. Thus three out of ten were affected.

Two features are worthy of mention. Firstly, it is remarkable that five brothers should have married granddaughters or great-granddaughters of II-1. Secondly, the fact that all of these had polydactylous descendants attests to the frequency with which the character occurred among his progeny. It is to be noted that a completely polydactylous individual (VIII-1) appears in a line in which there is no record of an affected ancestor. This is probably to be attributed to incomplete information, but similar instances occur elsewhere, and will be discussed later.

Family 3

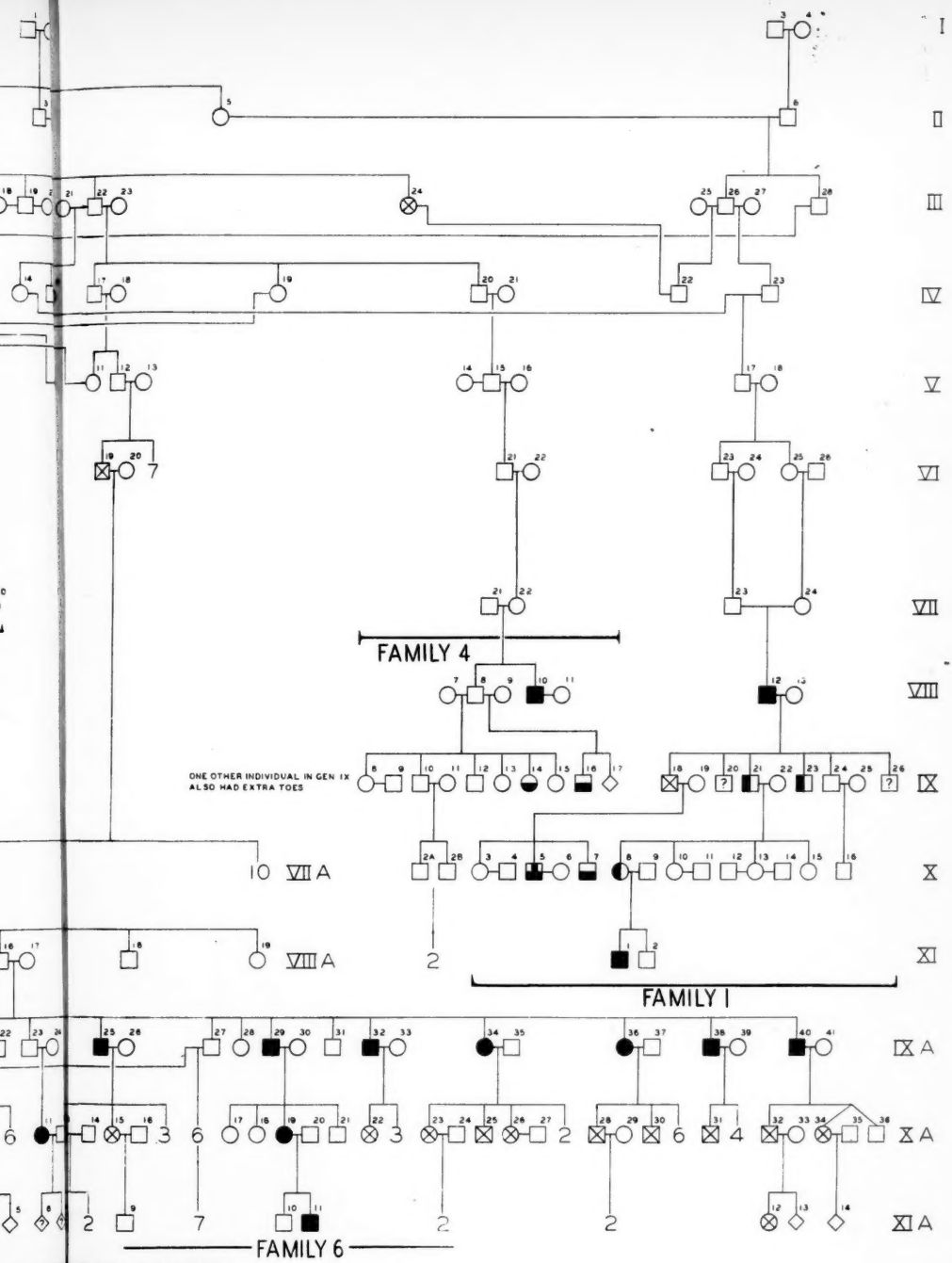
In 1876 a girl (X-1) entered the Massachusetts General Hospital for the re-



SIX RELATED POLYDI

Fig

An individual born in England about 1620 (II-1 in the chart) is pro
America. Black symbols indicate individuals who are polydactylous in both
half of symbol) or feet (lower half of symbol). The symbol X indicates
ing as to which members are affected. The great variation in the expressi
this pedigree. For further details regarding symbols used see page 46.



POLYDACTYLOUS FAMILIES

Figure

chart) is progenitor of extra-fingered individuals living in many parts of North us in both hands and both feet. Partial symbols indicate polydactyly of hands (upper indicates person known to be polydactylous but regarding whom information is lacking e expression this characteristic is one of the interesting and perplexing features of e 46.

moval of supernumerary fingers. A report[3] of the case was published at the time, and the present director of the hospital kindly furnished a copy of the hospital record. The history of the case was as follows:

Supernumerary fingers and toes have been hereditary in her family as far back as can be remembered. Her only sister (X-2) had them. Her father (IX-3), two of his sisters (IX-5 and 6) and one brother (IX-2) had them, a sister (IX-4) and a brother (IX-1) being free from them. His mother (VIII-3) had them. Her father (VII-8) and three of his family and their mother (VI-7) had them. Further back than this could get no information.

The supernumerary fingers were removed under ether anaesthesia. On the left hand the extra digit articulated directly with the side of the metacarpal of the little finger and was merely disarticulated. On the right hand the finger articulated with an extra metacarpal bone which sprouted from the metacarpal bone of the little finger; this was sawn off.

The hospital record contained the patient's name and address. The names of her parents and sister were obtained from census records. Available genealogies of the family failed to include them, but by reference to local vital records it was possible to establish the identity of her grandparents and great-grandparents. The latter were recorded in genealogies from which the pedigree was completed and the connection with the ———— family disclosed. It was not possible to document every relationship, but there seems to be little doubt that the pedigree is correct for the data obtained from these various sources are complementary.

Two features of this pedigree are noteworthy. One is the high proportion of affected members; in three complete families having a polydactylous parent, 10 out of 15 individuals show the character. The other is the degree to which these individuals are affected, all being completely polydactyl.

Family 4

The files of the Genetics Record Office were also the source of the following statement, which is an extract from a letter written by the the woman indicated as IX-8:

We are ————s and they are a great family for that (i.e., polydactylism). My father's (VIII-8) only brother (VIII-10) had twelve fingers and twelve toes. He had no children, but of my father's eight, three had extra toes or rudiments, and of his ten grandchildren, one.

Some additional information has been obtained from a brother (IX-10) of IX-8, who wrote:

I am sorry I do not know exactly the number of instances occurring in my own generation or the next. I know that as a surgeon I removed two auxiliary little toes from my half-brother (IX-16), my father's son by his second marriage. My sister, IX-14, also had some extra digits, although I do not know just where they were located. I had not heard of any member of the next generation thus affected but IX-8 refers to one case. . . . . neither of my boys (X-2A and 2B) show polydactylism nor has it occurred in the case of my two grandchildren.

There is an excellent genealogy of this family, compiled by VIII-8. His mother (VII-22) bore the family name of II-1 and was presumably responsible for the introduction of the character into this family, but the genealogy gives no information concerning her ancestry beyond her father's generation. Fortunately a local history contains a genealogical sketch which establishes the position of her branch of the family in the greater pedigree.

There are four affected offspring out of 10 in the two families here represented. No information is available concerning the parents of VIII-8; he was presumably normal, but he nevertheless had polydactylous children.

Family 5

The information concerning this pedigree was obtained from a communication published in an English journal more than 100 years ago. Its author examined the individuals indicated as VI-13 and VII-17, and from the former obtained data concerning other members of the family. The following quotations are particularly interesting:

VII-17, a native of ..... North America, has a supernumerary little finger growing from the outside of the metacarpus of each

hand, and a supernumerary little toe upon the outside of the metatarsus of each foot. These extra fingers and toes are all completely formed, having each of them three perfect phalanges with the ordinary joints and well shaped nails.

VI-13, the father of VII-17, has five fingers and a thumb upon each hand, and six toes on each foot; he has also five metacarpal bones in each hand and six metatarsal bones in each foot. The extra limbs have distinct flexor and extensor tendons.

The wife of VI-13 has no peculiarity in her limbs. During the existing marriage, she has borne eight children, six sons and two daughters. Four of these sons inherit the peculiarity of their father more or less complete, while the two daughters are free from the family mark, as well as two of the sons, namely the fourth in succession who was a twin, and the eighth.

The eldest son of these parents, VII-12, has only five toes on one of his feet, but the other foot, and both his hands possess the extra limb. . . .

Besides the persons I have mentioned this hereditary redundance of limbs has been attached to the little fingers, and to the little toes of several of the ancestors of the family. The mother (V-8) of VI-13 brought the peliarity into his family. . . . she however had not the extra finger on one of her hands; the other hand, and her feet were similarly marked with those of her son VI-13.

V-8 inherited these supernumerary limbs from her mother (her family name is given), and she had five fingers and a thumb upon each hand, and six toes on each foot.

The marriage of IV-12 with IV-13 produced eleven children, whom V-8, who was one of the eleven, reports to have been all completely marked: but the present family are unacquainted with the history of the other ten branches, and they do not possess any knowledge of their ancestors beyond IV-13....

The true connection between this pedigree and that of the ———— family is not wholly certain. VI-13 stated that his grandmother was polydactyl, and her surname as he gave it is borne by this family. The meager genealogical information available seems to indicate that he omitted a generation, however, and that his great-grandmother, III-14, actually possessed these attributes. This woman, by her marriage to III-15, had nine children including a son, IV-12, and a daughter whose name was the same as that of V-8. IV-12 is known to have had eight children whose births are recorded in a single town, and a local history states that he came to the town "no doubt, with a family." Among these children was a daughter whose name was also that of V-8; it is assumed that she married V-9 for the pedigree constructed on this basis accommodates the data with the least difficulty. It may seem unlikely that VI-13 would make an error of this nature, but the genealogy reveals that he omitted one of his sisters and his youngest daughter as well.

The inheritance of the character in this family is also that of an ordinary dominant, with variation in expression. In two completed families having one polydactylous parent, eight out of 14 offspring are affected. The twins which occur in this family were presumably fraternal, since one was normal while the other was completely polydactyl.

Family 6

Though genealogies of the descendants of II-1 gave ample confirmation of the belief that many of these individuals were polydactyl, it was impossible to obtain any information concerning those in the earlier generations. Nevertheless, by great good fortune a most extensive pedigree of the character in one branch of the family was secured.

According to tradition in this branch the immigrant ancestor II-1 was polydactyl, as was his youngest son, III-22, and his great-great-grandson, VI-19. There is no record that any of the latter's twelve children were affected, but he had four polydactylous grandchildren, and three other grandchildren who were apparently unaffected nevertheless became parents of polydactylous children. In all, this pedigree includes 46 affected individuals distributed among 27 families and appearing in five out of six generations.

The most interesting feature of this pedigree is the marked irregularity of inheritance which it displays. If the tradition that VI-19 was affected is accepted, it may be seen that there are two lines in which the character first reappeared in a grandchild, three lines in which it first reappeared in a great-grandchild, and two lines in which it first reappeared in a great-great-grandchild. Particular inquiry was made con-

cerning the individuals who transmitted the character without being visibly affected themselves. No amplification of the original statements concerning VIIA-1 and IXA-14 was obtained, but it was learned that a photograph of VIIA-3 shows the only hand visible to be apparently normal. Both IXA-29 and IXA-32 are positive that VIIIA-3, VIIIA-14, VIIIA-16 and IXA-23 showed no evidence of extra digits. In spite of this all these individuals had polydactylous offspring. The family of VIIIA-16 is particularly notable; though he was apparently unaffected, eight of his twelve children were polydactyl, and IXA-29 "is fairly certain that all his polydactyl brothers and sisters had the full set, as did he, his daughter, and grandson." This problem is so important that it will be discussed later.

Twins appear twice in this pedigree. XIA-3 and 4, both of whom are completely polydactyl, are probably monozygotic, while XA-34 and 36, the former polydactyl, are fraternal twins since they are also of different sex.

Discussion

One aspect of the inheritance of polydactylism in man, namely, the reported disappearance of the character through outcrossing, warrants examination because of the attention paid to it by Gates.[6] He wrote as follows (p. 172):

> Ballowitz[1] quotes from the French literature (1863) the case of an isolated village in the Departement d'Isère, in which, through inbreeding, nearly all the inhabitants had six fingers and toes. Later, owing to increased communications, marriages with normals took place, and the extra fingers and toes in newborn children became smaller and fewer, finally disappearing altogether. This is a good example of the weakening and disappearance of an abnormality through exogamy, but brachydactyly does not appear to be affected in this way. If such weakening of a character like hexadactyly can take place through exogamy, it is an important hereditary principle which requires further elucidation, especially in comparison with conditions like brachydactyly, where no weakening effect is observed even after many generations of outcrossing.

Gates also referred to a paper by Castle[4] which appeared in 1906. This dealt with polydactylism in guinea pigs, but bore a postscript concerning the condition in man from which Gates quoted as follows: ". . . . polydactylism usually makes its (recorded) appearance in some noteworthy form, it is transmitted more or less strongly through two to five generations, and then disappears, doubtless so weakened by repeated outcrosses that its manifestations, if any occur, are no longer observed."

The case from the French literature which Gates mentions has been criticized by Baur, Fischer, and Lenz:[2]

> In the literature of polydactylism, we find again and again the statement that in a southern French village (Izeaux in the department of Isère) polydactylism was so widely diffused that at last the majority of the inhabitants became affected. Inbreeding was said to be the cause of this; for as soon as the inbreeding ceased, the polydactylism disappeared. R. Sommer (Ueber Familienähnlichkeit, Vienna, 1917) has shown that this story, for which a French writer named Potton was primarily responsible, is unfounded. Besides, inbreeding has no special effect in the case of dominant taints.

It is interesting that this story also influenced Castle. In answer to a request for his present opinion on the subject, Professor Castle has kindly written me as follows:

> The passage quoted by Gates in his *Heredity in Man* is taken from a postscript to my 1906 paper. It does not represent my present views about the case accurately. I expressed the view quoted (1) under the influence of the paper by Ballowitz ('04) cited in my bibliography, and (2) because of the irregularity observed in the inheritance of polydactylism in guinea pigs. . . . The idea which at that time I entertained tentatively that a mutant character might be subject to modification by outcrossing has since been shown to be, if not erroneous, at least requiring explanation or interpretation.

The present pedigree also offers evidence that weakening and disappearance of the character through exogamy does not occur. The polydactylous individuals which it includes are all descendants of the individual indicated as II-1. For this reason, and because of the tradition that polydactylism occurred among his English forebears, there seems to be no reason to doubt that he and many of his sons and daughters were polydactyl. He was born about 1620. The character has thus been handed down through nine

generations of his descendants over a period of more than 320 years. Even in the latest generation the affected individuals may be completely polydactyl, and the extra digits may be perfectly developed. In this pedigree therefore polydactylism seems as persistent as the brachydactylism to which Gates refers.

It is nevertheless true that the manifestations of the gene responsible for this condition are not the same in all branches of the pedigree, and a comparison of them reveals considerable individuality.

Family 3 displays complete regularity in inheritance, a high affected : normal ratio (2 : 1), and complete uniformity in pattern. Families 1 and 5 likewise display complete regularity in inheritance, but the ratios (7:8 and 8:6) approach the theoretical proportion for the offspring of parents one of whom is heterozygous. There is considerable variability in pattern. Families 2 and 4 show apparent irregularity in inheritance, a low affected : normal ratio (3:7 and 3:5), and similar variability in pattern. As a group these five families display a ratio of exactly 1:1.

In Family 6 detailed descriptions of the majority of affected individuals are lacking, but the information available indicates uniformity of pattern. The ratio of affected : normal individuals is low, being almost exactly 1:2. This is attributable at least in part to the fact that seven individuals who are represented as normal in the chart nevertheless had polydactylous descendants. If they are assumed to be genotypically polydactyl and are added to those visibly affected, the ratio becomes 1:1.7.

When the entire pedigree is considered we find 38 complete families which include 77 affected offspring and 122 which were apparently normal, giving a ratio of approximately 1:1.6. If a correction similar to that applied to Family 6 is made, the ratio becomes about 1:1.4.

It may be objected that the assumption that apparently normal individuals who produce polydactylous offspring are themselves genetically polydactyl is unwarranted. In this connection it may be pointed out that some polydactylous individuals exhibit extra digits on one side of the body while the other side is apparently normal. In others only a single extremity may be visibly affected. It does not seem unreasonable to expect that some individuals may appear entirely normal while possessing the gene responsible for the condition. Furthermore, in other hereditary conditions affecting the hands and feet it has been shown by radiography that some individuals regarded as normal were actually slightly affected.[5]

The irregularity in inheritance, which is to be seen in Families 2 and 4 but which is especially frequent in Family 6, is perhaps the most interesting feature of this pedigree. The appearance of a polydactylous individual in a line which has been free from the condition for one, two or three generations would seem to indicate a recessive heredity, but other considerations show that this cannot be established. As stated above, the ratio of affected : normal offspring of parents one of whom is presumably heterozygous is exactly 1:1 in Families 1-5, taken as a group. This is exactly the ratio one would expect if the character is a pure dominant, and even the ratio of 1:1.7 for Family 6 and that of 1:1.4 for the pedigree as a whole are not sufficiently different from the theoretical ratio to alter the opinion that the character is fundamentally a dominant one.

If this interpretation is correct, the irregularity is the result of variability in the effects produced by the gene involved, and since similar variability has been observed in the effects produced by other genes it is pertinent to cite a few examples.

Mohr and Wriedt[9] studied an extensive pedigree of brachyphalangy in which two distinct expressions appeared. They attributed this variation to the action of a modifying gene, but since the variability of expression of the present character is considerably greater, it does not seem likely that such specific modifiers are responsible.

Hefner[7] described a case of symphalangism which showed irregularity in

expression and inheritance, and made the following suggestions:

> The widely expounded idea of the localization of specified factors in definite genes must in this instance be modified or extended for application to the observed behavior of the character here presented. Such a factor must itself be capable of modification to produce the various aspects of the trait, since symphalangism presents a series of variations and even a disturbance of the characteristic bilateral symmetry. It is thus a logical deduction to assume that the gene itself is an organization subject to changes which are here expressed as a variable trait. The nature of such changes and the reasons for their occurrence must be intimately associated with the primary cause of the mutation itself.

More recently Hefner[8] has described a case of hereditary polydactyly associated with extra phalanges in the thumbs. In this pedigree the polydactylous condition appeared in four members of one generation after being absent during three generations. He makes no attempt to explain this phenomenon.

In the letter previously mentioned, Professor Castle further wrote as follows:

> The current (and I believe correct) interpretation is this. A mutant character is primarily the result of a gene mutation, ordinarily mutation in a *single gene*. This gene is transmitted *unmodified* to such offspring as receive it, but its phenotypic expression may change through the influence of other genes which may become associated with it in consequence of outcrosses. Thus the *expression* of a gene is subject to modification by associated genes, but the gene itself does not change unless by a new mutation.

The variability in expression observed in the present pedigree, and the differences between the component pedigrees seem best accounted for by this conception of interaction of one gene, in this instance a dominant one, with other genes of the milieu. At the same time it should be admitted that their total effect may be subject to modification by external influence during the period of development when the digits are being determined.

If the apparent irregularity in inheritance is the result of a failure of a dominant gene to produce a recognizable effect, it is evident that it is misleading to speak of the skipping of generations, even if this phrase is merely intended to imply that an individual in an affected line is not visibly affected. The terminology is especially confusing to the layman and creates scepticism concerning the applicability of the principles of heredity to man.

The study of human heredity would be greatly aided if genealogical data connected with new pedigrees of this and other characters were collected, deposited with an appropriate agency, and thus made available to other investigators. In this way relationships might be established when they exist, and a better understanding of the operation of hereditary factors in man would certainly result.

Summary

1. A genealogical study of six families in which polydactylism occurs has shown that all are included among the descendants of an English settler who arrived in New England before 1644.

1. It is therefore possible to depict their relationship in a single pedigree involving ten generations and including 90 polydactylous individuals, many of whom are now living in widely separated parts of North America.

3. The polydactylous condition may be bilateral or unilateral and may affect the hands, feet, or both hands and feet. So far as can be determined a single supernumerary digit appears on the postaxial border; it may closely resemble the fifth digit or may be a mere fleshy appendage. Intermediate conditions also occur.

4. The genetic factor responsible for this polydactylism is believed to be a dominant gene whose expression is highly variable.

5. This variability is attributed to the influence of the genotypic milieu into which this gene is introduced, and possibly to the modifying effect of external influences during development.

6. There are some instances in which apparently normal individuals are the parents of polydactylous offspring. It is believed that such individuals are genotypically polydactyl, though no somatic expression of the gene is evident.

7. It is hoped that more attention will be devoted to the collection and preservation of genealogical data associated with new pedigrees of this and other hereditary characters.

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EUGENICS AND MORALE

EUGENICS is perhaps at its best and most hopeful as a catalyst privileged to give new insights and sounder direction to a number of human activities. As a corollary to this, one of the major compensations of being a eugenist is the unexpected ways one finds oneself in the presence of unexpected and stimulating intellectual bedfellows. Recently one of the plaints of the eugenist and human biologist has been that eugenics is a long-term business which has very little direct contact with the urgent life-and-death world we find ourselves precariously living in today. What profit the survival of superior germplasm if the Democracies get caught in a further chain of too little-and-too-late in winning the war or the peace? Who especially cares whether the differential birthrate be out of kilter if Hitler were to succeed in his plans for a "thousand years of Neuropa"? Possibly the urgencies of the moment have blinded us to certain direct and practical ways in which a eugenic point of view can contribute to the winning the war and the peace.

Some eugenists have sensed the possibility that the truth about human biology has elements of war-making value, but these prospects have not yet been effectively formulated. Important leads for developing this point have recently appeared from a wholly unexpected quarter. A small group of social psychologists have been for several years concerned with the implications of applied psychology in a changing world. The 1942 world being a world at war, the current yearbook of the Society for the Psychological Study of Social Issues is appropriately devoted to "Civilian Morale."* Several chapters of this book turn out to have important eugenic implications, and suggest ways in which the eugenist can take an active and significant part in the war effort. The eugenic meat is in two of the sections: that on war aims, and that devoted to children and morale.

The eugenic implications of the latter topic might be thought to be a bit far-fetched, but such is emphatically not the case. The kind of people who have high morale are the kind of people the eugenist is interested in adding to the fabric of society. As Dr. Lois Murphy vividly points out, there are many things in our social structure which tend to engender problem-children destined to grow into problem-adults five or ten years hence. It follows that "attention to adults and to economic problems alone

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Watson, Goodwin, Editor: *Civilian Morale*, Second Yearbook of the Society for the Psychological Study of Social Issues. A Symposium, with contributions by 19 cooperators. Pp. xii-463. $3.50. Houghton Mifflin Company. New York, etc. 1942.

is not enough. The roots of many of these adult difficulties in the future lie in the basic experiences of children today —experiences of frustration and insecurity that are producing unsocial, distorted personalities maturing into inadequate adulthood year by year." Such forces must also work against a eugenic society in various ways. One of the most important effects would be that in proportion as such forces corrode the mental and physical qualities of our population, this will leave only a tougher and more highly-endowed genetic residuum available for military service. This intensified selection of the best thus adds to the dysgenic effects of war. In proportion as the Selective Service must find suitable sacrificed material in a smaller proportion of the population, the destructive influence is the more deadly. Churchill's "never have so many owed so much to so few" has tragic genetic implications, which remain true even if this has become a war of civilians as well as of soldiers. Anything which tends to spread the selective availability for the sacrifice is a definite eugenic gain.

Another important eugenic consideration is that it is not possible to decide who is genetically who in human populations, unless a reasonable equality of environment is achieved. Only when we succeed in preventing the environmental synthesis of distorted, disordered, and inadequate adults can we really begin to cast up our genetic accounts. Surely such matters are of vital concern to the eugenist. Dr. Murphy's pretty grimly sketched backdrop for the slogan "Life, liberty and happiness for children NOW" reminds us that pre-war realities left much to be desired. Yet surely the realization of that slogan is a basic war and post-war objective which eugenists and morale-ists are at one in wishing to see realized. And its realization will do as much as can any one factor to bring to fruition that New Horizon world which is the hope of all free people—R. C.

♦

Biology for Sociologists

To the Editor:

Your review of *Society Under Analysis* strikes me as not directed toward the objective which you profess to share with me—a closer relationship between the sciences and the social sciences. There are points at which I might retort in kind; that is to say, unkindly, but the question that seems important in my mind is, what will be the effect of such a review? I had a tougher time getting sociologists to write chapters you reviewed than any others. Sociologists do not want to write biology. Some are afraid to, and many of them do not consider biological facts to have any social significance. Do you prefer that sociology students get "anti-biology" to what you think of as the inaccurate biology in *Society Under Analysis?*

Knowledge of a field by members of another discipline is necessarily incomplete. Specialization assures that. To expect anything else is to be unrealistic. Do the writers whom you reviewed know less of biology than almost any biologist knows of sociology?

At any rate, by tending to scare away such sociologists as have an appreciation for the importance of biology you tend to saddle on sociology students an attitude under which biology is disparaged. If your brand of cooperation is general, then after the physicists and the chemists and the geographers and the geologists and the economists and the psychologists get through with me, even I may wish to had left the sociology students in their isolated world. Rapport is desirable, I think, but approaches from one side alone may not be able to bring it about.

Elmer Pendell

The means of achieving rapport cannot be ignored. Surely there is a responsibility of sociologists to write reasonably accurate biology. If that is not feasible should not the cooperation of a competent and well-informed biologist be somehow obtained? A fairy-tale biology can never help the embryo sociologist to an understanding of the basic realities on which his discipline must be grounded. That a textbook is "objective," "authoritative," and "up-to-date" would seem to be a primary responsibility of editor and publisher. When claims that this is so are not supported by the context, it is surely worthy of note.—Ed.

HEREDITY AS AN AETIOLOGICAL FACTOR IN MALOCCLUSION

As Shown by a Study of the Dionne Quintuplets*

NORMA FORD, and ARNOLD D. MASON†

MALOCCLUSION means that the jaws do not fit together perfectly. The determination of the underlying causes of this condition constitutes one of the main dental problems at the present time. Various hypotheses are advanced to account for these widespread disparities in dental architecture, but comparatively little positive evidence is available to support any of them. Heredity as an aetiological factor has been suggested by many workers, including Chapman[5], Hellman[9] and Brash[1], but the great complexity of the problem, in which multiple hereditary factors are probably involved, has made it difficult to assemble data adequate for statistical analysis. The most promising approach to the problem is through the study of occlusion in identical and fraternal twins. The value of such data has long been recognized, but until recently it has been open to serious question, since the diagnosis of twins into one-egg and two-egg sets was itself uncertain.

In the last few years twin diagnosis has become comparatively reliable through systematic comparisons of anthropological measurements, dermatoglyphic patterns, and blood groups, supplemented by records such as foetal membranes and taste reactions. For higher multiple sets the same methods of diagnosis are followed and the value of the data derived from them becomes increasingly significant as we apply these techniques to triplets, quadruplets and quintuplets.

Since the Dionne quintuplets are known to be an identical set [6,11], and since their dentitions are classed in the malocclusion series, a rare opportunity now presents itself to determine whether hereditary factors are involved in the aetiology of malocclusion.

Moreover, if heredity is a factor in malocclusion, it then follows that the condition, exhibited clearly in the permanent dentition, probably was present not only in the deciduous stage but even earlier in development. The present study attempts to trace these progressive changes in the Dionne quintuplets and to show that the irregularities of their permanent dentition are inherited and were foreshadowed in the deciduous arch.

Materials and Data

Unusually good material was available for this study, since moulds of the dentitions of the Dionne quintuplets have been taken annually, and in addition, careful records of the time of eruption of all their teeth have been kept. The shed deciduous teeth have been preserved. It is surprising to find that very few comparable series of records (of even single-born children) have been kept in any of the research centers. An exception, however, is the Merrill-Palmer School in Detroit. To this institution and to Dr. S. J. Lewis in particular, we are much indebted for the privilege of extracting data from their extensive series of dental records.

A preliminary account of the deciduous dentitions of the Dionne quintuplets was published by Mason[12]. The present study is based on the examination of six annual models (from 2 to 7 years), including the first twelve permanent teeth.

*A contribution to the dental studies of the Dionne Quintuplets.

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Sequence in the Order of Eruption of Teeth

A standard of measurement for the development of dentition is the sequence of eruption of the teeth. Hellman[9] has shown, in the case of the permanent dentition, that there is a striking difference in the sequence of eruption between normal occlusion groups and malocclusion groups. Children with malocclusion begin to erupt their permanent teeth earlier and finish the process later than do those with normal occlusion. Moreover the first tooth of the permanent set to erupt in the malocclusion group is on an average the lower central incisor, while in the normal group it is the lower first molar. Besides in the malocclusion group the upper first molar precedes its lower partner. The sequence of eruption is therefore a useful standard of measurement in the study of malocclusion.

Succession of Eruption of the Permanent Dentitions of the Dionne Quintuplets

Although the eruption of the permanent dentition of the Dionne quintuplets at seven years of age is far from complete and involves a consideration of only twelve teeth, a review of their succession shows clearly a developmental pattern of the malocclusion series. Times of eruption for the five children are summarized in Table I and compared with Hellman's averages. From these data it will be noted:

(1) that the first permanent teeth of the quintuplets to erupt are consistently the lower central incisors (with an average eruption age of 5.63 years);

(2) that the upper first molars have preceded the lower first molars;

(3) that the average eruption time (5.63 years) of the first permanent teeth is not only earlier than the average for normal occlusion (6.81 years) but even ahead of the average for malocclusion groups (6.05).

The delayed eruption of the lower first molars of the Dionne quintuplets is an important feature of their developmental pattern. Usually the first molars erupt before any of the lateral incisors in both the normal and malocclusion groups (Table I), but in the case of the quintuplets (in so far as these teeth have appeared) the reverse is the case.

Comparisons of Developmental Patterns of Eruption

The fact that a common pattern in the order of eruption of the teeth can be traced among the Dionne quintuplets suggests that this pattern may be an inherited one. To test this thesis comparisons were made using data from 37 series of records on file at the Merrill-Palmer School.

To compute the percentile difference in the orders of eruption of the teeth of any two individuals the following method was devised: First the data were recorded according to the year of eruption, as shown in Table II. Differences in time of eruption of the teeth were then counted, giving a value of 1 for each tooth-difference. For example in the cases cited in Table II, there was a difference in the fifth year in the eruption of the two lower median incisors (two points of difference); in the sixth year of the two upper median incisors, the right upper lateral incisor, and the two lower lateral incisors, making a total of five points of differences. The total difference for twenty-eight permanent teeth amounted to 60.7%.

Using this method the Dionne quintuplets were compared among themselves, as ten pairs of twins, and showed an average difference of 25.8% (Table III). In the records of the Merrill-Palmer School there were data on one pair of identical twins, one pair of fraternal twins, nine pairs of siblings and twenty-five single-born children. The latter were compared as 78 random pairs of girls and 66 random pairs of boys. The percentile differences between these various pairs are shown in Table III, the comparisons being based on (1) twelve teeth and (2) on twenty-eight teeth. The general trend in the numerical values shows for the twenty-eight teeth that the lowest percentile difference is between the identical twins (32.1), a

higher one between the fraternal twins (50.0), still higher for siblings (56.7) and the maximum for random pairs (♀ ♀ 67.9, ♂ ♂ 73.9). These numerical values are of an order which would be expected if heredity is a factor in the pattern of eruption. Since the average difference between the Dionne quintuplets is 25.8% it indicates that their developmental pattern is an inherited one.

Succession of Eruption of the Deciduous Dentitions of the Dionne Quintuplets

Too frequently in the past the mistake has been made of associating malocclusion with the permanent dentition only, but more recently opinions have been changing and factors are now recognized which operate at an early age, and probably before birth. Brash[1] has pointed out that "it is clearly of the utmost importance to inquire what is the earliest possible stage at which they (irregularity and malocclusion) may be recognized as such, and at which they may be determined."

Since the permanent dentitions of the Dionne quintuplets show an inherited developmental pattern characteristic of malocclusion, it may well be expected that some comparable pattern occurs in the succession of their deciduous teeth. Unfortunately no published data are available on the eruption of deciduous teeth in malocclusion groups. (We are at present assembling this material.) In the meantime a comparison has been made in Table IV of the sequence of eruption of the deciduous teeth of the Dionne quintuplets with averages computed by Boas (Hellman[8]) and Robinow *et al*[13]. Considerable discrepancy exists between these two series of means, those of Robinow giving consistently younger ages. Compared with the latter series the deciduous teeth of the Dionne quintuplets are all retarded in eruption, but compared with the former series this is not so. From a study of Table IV the following three points may be noted:

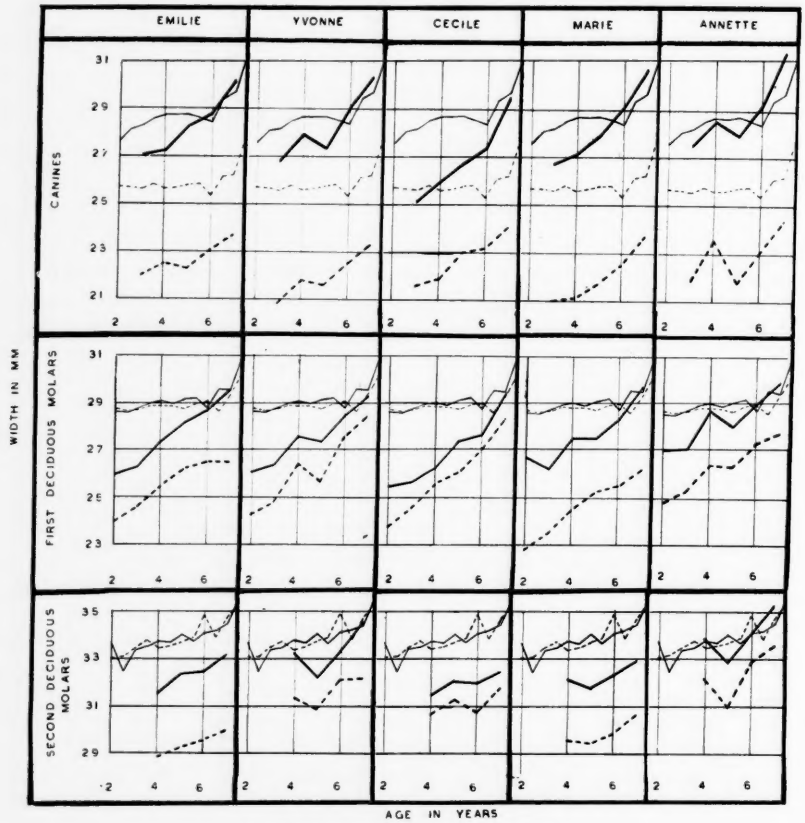
(1) On an average the upper central incisors of the quintuplets erupted before the lowers, although there is considerable variation in time of eruption among the five children. (2) On an average the upper central incisors of the quintuplets are precocious in their development as compared with Boas (12.9 months instead of 13.6), while the lowers are retarded (13.3 months instead of 10.7), although both ages fall within the limits of the standard deviation. (3) The most significant difference between the quintuplets and the average for girls is in the late eruption of the second deciduous molars (36.7 months for the uppers, instead of 28.6±4.9; and 36.9 months for the lowers instead of 27.9±6.0). Both these times of eruption lie beyond the limits of the standard deviation as given by Boas and Robinow.

Without adequate data for comparison, little more can be said at the present time, except to point out that the general trend of eruption of the deciduous teeth of the Dionne quintuplets is consistent with the growth pattern of malocclusion as seen in the permanent dentition, in so far as the eruption ends later than in the normal groups. The delayed completion of the eruption is due mainly to the marked retardation of the second deciduous molars.

Malformation of the Mandibular Molars of the Dionne Quintuplets

The second deciduous mandibular molars of the Dionne quintuplets were not only late in appearing, but after eruption showed distinct anomalies in form. In place of clear-cut fossae and typical developmental grooves the crowns of the teeth were flattened and crumpled in the centre, with the appearance of having grown under pressure. This irregularity of the enamel made it exceedingly difficult to locate with accuracy certain points, such as the central fossae.

Grüneberg[7] found a similar condition in the unerupted teeth of a grey-lethal mutation in the mouse and was able to demonstrate by histological studies that the tooth anomaly was due to the lack of bone absorption in the socket enclosing the tooth germ. In fact the bone absorption in the grey-lethal mutation



WIDTH OF DENTAL ARCHES

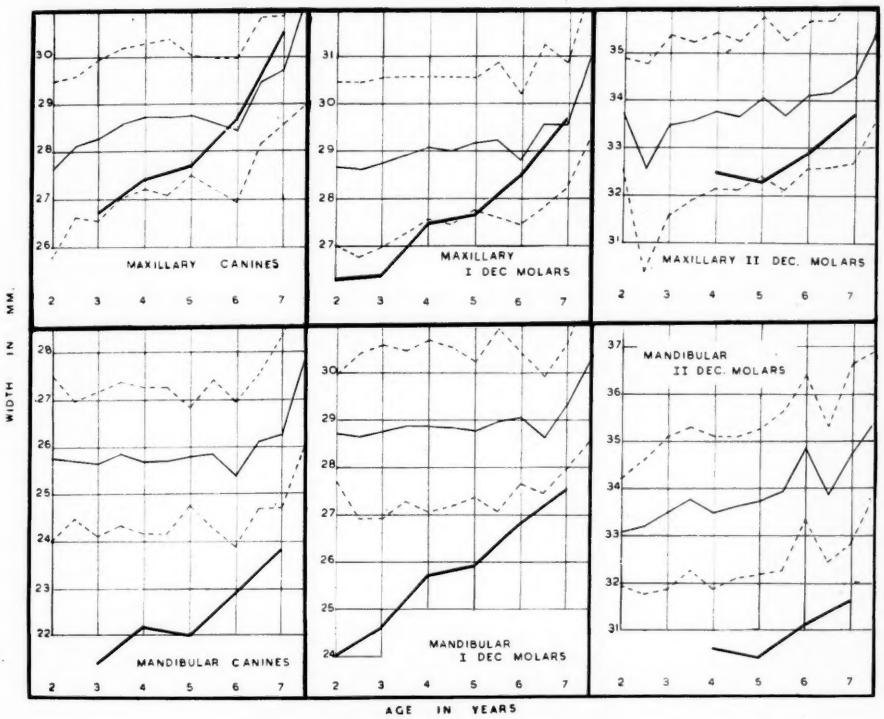
Figure 7

The widths of the arches of the Dionne quintuplets are shown in the heavy line and heavy dash. These are compared with the same measurements in a group of 170 children compiled by Lewis and Lehman.[10] The solid lines represent maxillary widths and the dotted lines, mandibular widths. Note that the development of the quintuplets' upper jaws (maxillæ) more closely approaches the mean than the development of the lower jaws (mandibles). This disparity in development is obviously an important factor in the development of malocclusion, wherein the teeth of the upper and lower jaw are not in normal apposition.

was so far reduced, that no teeth were able to erupt. Grüneberg points out that the ability of bone to react to the pressure of the tooth germ is evidently rooted in hereditary factors and he states that "in the hierarchy of causes the bone anomaly is nearer the original gene action than are the tooth shape anomalies dependent on it." An important conclusion reached by Grüneberg is that "the relation between stimulus and response is not direct, as assumed hitherto, but subject to conditions based in the hereditary constitution of an animal." Briefly this view is expressed as follows:

Stimulus⟶ Hereditary basis⟶ Response
(Pressure) for response (Absorption)

It would seem, therefore, that the retarded eruption of the molars in the quintuplets may similarly be due to some inherited disturbance of bone growth



GROWTH OF DENTAL ARCHES

Figure 8

The mean width of the dental arches of the Dionne quintuplets from three to seven years of age are shown by the heavy lines, compared with mean width (light lines) and standard deviations (dotted lines) for the 170 children reported by Lewis and Lehman.[10] The varied increases in width of different parts of the arch throughout the period studied show that malocclusion is a development process which has its beginnings in early infancy.

of the mandible. That such a hypothetical disturbance is a reality seems to be shown by the following description of the growth of the dental arches.

Measurement of Growth Changes in the Widths of the Dental Arches of the Dionne Quintuplets

An attempt has been made to measure as accurately as possible the widths of the dental arches of the Dionne quintuplets during their period of growth from two to seven years. The method devised was to obtain a magnified image of the model of the teeth by using a large upright camera (part of the photographic equipment of the Department of Zoology). The image was focussed on a ground glass plate and accurately magnified to twice the diameter of the model. In making the necessary adjustments for enlargement, a round glass scale (made by Adam Hilger Ltd., London) was laid on the model so that it fitted the arch and the measurement of its units on the ground glass was taken through a second glass scale.

The points on the teeth to be measured were carefully marked with small red dots, made with a well pointed pencil. These showed up clearly under strong illumination and their positions were carefully recorded on tracing paper by using either a fine pen or a finely

TABLE I. Age in Years at Time of Eruption of Permanent Teeth of the Dionne Quintuplets, Compared with Hellman's Standard of Succession.

Group			Hellman '38 (for girls)		Dionne Quintuplets											
			Unocclusion	Normal Occlusion	Average for Quintuplets		Emilie		Yvonne		Cecile		Marie		Annette	
							Yr.	Mo.	Yr.	Mo.	Yr.	Mo.	Yr.	Mo.	Yr.	Mo.
Central Incisor	Upper		6.80	7.58	6.39		6.71	6.40	6.36*		6.36	6.51	6.20	6.48	6.10	6.40
	Lower		6.05	6.95	5.63		5.49	5.64	5.80	5.74	5.80	5.58	5.49	5.75	5.68	5.54
Lateral Incisor	Upper		8.21	8.30	6.98+				7.09		6.85*	6.91	6.90		7.12	6.98
	Lower		7.15	7.75	6.62+		6.53*	6.85	6.64				6.53	6.53*	6.53	6.53*
First Molar	Upper		6.14	7.17	7.0+		7 year Model 1/2 Fr.	7 year Model Cusp	7 year Model cusp		7 year Model cusp	7 year Model 1/2 Fr.	7 year Model Cusp	7 year Model 1/2 Fr.	7 year Model Cusp	
	Lower		6.39	6.81			6 year Model 1/2 Fr.						6 year Model 1/2 Fr.			

* Time of eruption of tooth approximate. +Fr: erupted

TABLE II. Method of Computing Percentile Difference in the Order of Eruption of Permanent Teeth.

Name	Year of Eruption of Each Tooth								
	5	6	7	8	9	10	11	12	
Shirley C.		6	1	2	$3^{L}4^{L}L^{L}$	$5^{R}6^{R}$	7		Upper
		1.6	2		3.4.5^{R}	5^{L} 7			Lower
Tania P.		6.1.^{R}	2^{L}		3.4.5^{R}	5^{L} 7^{L}		7^{R}	Upper
		1	6.2		3^{L}	$3^{R}4^{R}$	$4^{L}5.7$		Lower
Differences	2	5	1	1	6	1	1	0	Total 17/28 =60.7 %

The numerals represent the following teeth: 1, median incisors; 2, lateral incisors; 3, canines; 4, first premolars; 5, second premolars; 6, first molars; 7, second molars. The superscripts describe a tooth on the right or left side.

TABLE III. Showing the Similarity in Order of Eruption of the Permanent Teeth of the Dionne Quintuplets, Compared with Twins, Siblings and Random Pairs.

Comparison Based on 16 Teeth (Central and lateral incisors and first molars)	Average Percentile Differences	Comparison Based on 28 Teeth (All permanent teeth, except third molars)	Average Percentile Differences
Dionne Quintuplets (Compared as 10 pairs of twins)	25.8		
Identical Twins (1 pair, ♀ ♀)	16.6		32.1
Fraternal Twins (1 pair, ♂ ♀)	8.3		30.4
Siblings, ♀ pairs ♀ ♀ (2), ♂ ♂ (2), ♂ ♀ (5)	57.4		56.7
Random Pairs ♀ ♀, 78 pairs	61.3	♀ ♀, 6 pairs	67.9
♂ ♂, 66 pairs	67.3	♂ ♂, 6 pairs	73.9

Data for twins, siblings and random pairs culled from the records of the Merrill-Palmer School, Detroit.

TABLE IV. Age in Months at Time of Eruption of Deciduous Teeth of the Dionne Quintuplets, Compared with Means and Standard Deviations.

Group	For Girls (Boas) Hellman '38	For Girls Robinow, Richards, Anderson, '42	Average for Quintuplets	Dionne Quintuplets									
				Emilie		Yvonne		Cecile		Marie		Annette	
				Yr.	Mo.	Yr.	Mo.	Yr.	Mo.	Yr.	Mo.	Yr.	Mo.
Maxillary Central Incisor	13.8±4.7	9.6±2.0	12.9	13.8	13.6	12.4	11.7	13.0	13.1	12.8	14.1	11.7	12.7
Lateral Incisor	16.8±4.4	11.9±2.7	15.6	15.8	17.3	15.8	16.6	13.7	14.6	15.8	15.4	14.7	15.8
Canine	21.9±4.4	20.1±3.2	23.4	26.8	27.0	23.3	24.1	24.7	26.0	23.5	24.2	23.8	24.7
First Molar	20.1±3.4	15.7±2.3	19.5	19.0	20.5	20.0	19.8	18.8	20.5	18.6	19.8	18.6	19.2
Second Molar	28.6±4.9	28.4±4.3	36.7	36.5	36.1	37.8	36.2	34.9	36.1	36.4	37.0	37.0	36.4
Mandibular Central Incisor	10.9±3.3	7.8±2.1	13.3	15.1	14.8	14.6	14.0	12.0	11.8	14.4	12.5	10.8	13.4
Lateral Incisor	15.9±3.5	13.8±3.8	15.8	16.4	16.3	16.0	15.8	14.8	14.4	16.1	15.1	16.2	16.0
Canine	22.3±4.3	20.2±3.4	22.9	25.3	24.7	23.8	21.8	22.3	22.8	22.2	22.4	22.3	22.8
First Molar	20.1±3.9	15.6±2.2	18.4	17.3	19.5	18.2	17.3	18.9	18.6	17.9	18.2	19.5	18.2
Second Molar	27.9±5.0	27.1±4.2	34.9	37.1	33.8	36.9	39.9	36.4	37.1	34.9	35.7	38.4	37.2

TABLE V. Births of Dental Arches of Dionne Quintuplets from Two to Seven Years of Age. (Deciduous points used in measurements are described in text) All measurements in millimeters.

Age	Name	Mandibular				Maxillary			
		Canines	I Dec. Molar	II Dec. Molar	Enlargement	I Dec. Molar	II Dec. Molar	Enlargement	
7 years	Emilie	30.2	29.6	33.2	23.7	26.5	30.0	22.1	52.1
	Yvonne	29.1	29.1	33.1	23.5	27.6	32.8	23.5	51.1
	Cecile	29.4	29.4	34.6	23.4	28.4	31.8	23.8	52.2
	Marie	30.8	29.7	35.0	23.9	28.3	30.7	24.4	54.8
	Annette	31.5	30.0	35.5	24.4	27.8	33.6	25.1	52.9
6 years	Emilie	29.6	29.7	32.5	23.1	26.5	29.6	22.3	51.8
	Yvonne	29.1	29.5	33.0	22.5	27.6	32.1	23.0	50.6
	Cecile	29.4	29.4	32.3	22.3	27.6	30.8	23.0	51.3
	Marie	29.2	29.4	32.5	22.8	27.6	30.6	23.6	52.4
	Annette	29.5	29.1	34.1	23.1	27.4	33.0	24.1	51.0
5 years	Emilie	29.3	29.2	32.4	21.8	26.2	28.3	22.5	51.3
	Yvonne	27.4	27.4	32.4	21.3	27.4	31.5	21.9	50.3
	Cecile	28.6	27.6	32.1	21.6	26.3	31.5	21.9	51.3
	Marie	29.2	28.3	32.8	22.3	27.6	32.2	23.1	51.3
	Annette	29.0	28.2	32.9	22.4	27.6	32.9	23.1	52.2
4 years	Emilie	27.3	27.4	31.6	22.5	27.4	31.6	22.5	51.6
	Yvonne	27.4	26.3	31.5	21.9	26.3	31.5	21.9	51.3
	Cecile	26.0	26.3	31.5	21.1	26.3	31.5	21.1	51.3
	Marie	27.6	27.6	32.2	22.0	27.6	32.2	22.0	52.2
	Annette	27.6	27.2	32.9	22.4	27.6	32.9	22.4	52.2
3 years	Emilie	27.1	26.3	28.6	22.0	24.6	28.6	22.0	50.6
	Yvonne	26.8	26.4	28.6	20.6	24.6	28.6	20.6	50.6
	Cecile	26.2	26.3	28.6	21.0	24.6	28.6	21.0	50.6
	Marie	27.2	27.2	28.6	22.4	25.4	28.6	22.4	50.6
	Annette	27.6	26.0	28.6	21.6	24.6	28.6	21.6	50.6
2 1/2	Emilie	26.1	26.1	28.6	24.0	24.6	28.6	24.0	54.0
	Yvonne	25.8	25.8	28.6	24.3	24.6	28.6	24.3	54.3
	Cecile	25.2	25.8	28.6	22.0	24.6	28.6	22.0	52.2
	Marie	26.2	26.2	28.6	23.4	24.6	28.6	23.4	52.2
	Annette	26.6	25.6	28.6	22.5	24.6	28.6	22.5	52.9

TABLE VI. Losses in Width of Dental Arches of Dionne Quintuplets.

Name	Age (Years)	Mandibular			Maxillary			
		Canines	I Dec. Molar.	II Dec. Molar.	Enlargement.	I Dec. Molar.	II Dec. Molar.	Enlargement.
Emilie	5					22.3		
	4					22.5		
	3				21.6	25.7	30.9	
	2 1/2				21.6	26.4	31.4	
Yvonne	5							
	4							
	3						30.8	
	2 1/2						31.3	
Cecile	5							
	4							
	3						29.5	
	2 1/2						29.6	
Marie	5							
	4							
	3	27.4	27.4	32.4				
	2 1/2	27.4	27.6	33.3				
Annette	5							
	4							
	3	26.3		31.8				
	2 1/2	26.8		32.2				
	5	30.0	30.1	32.9				
	4	29.6	29.8	33.9				
	3				21.6	28.4	31.0	
	2 1/2				25.8	28.5	32.2	

pointed lead pencil, and by marking the exact center of the red dot. This center was picked out with the aid of a "linen counter lens."

All records were traced in quadruplicate. Two observers* independently made the tracings and subsequent measurements and the results showed that the readings were reproducible. The average standard deviation was less than one-half millimeter, and this error was reduced by half in the final calculations of the actual width of the dental arch.

The measurements of the arch were taken between points of functional occlusion on the upper and lower jaws, as suggested by Hellman for studies at the Merrill-Palmer School.[10] The distances measured were on the upper arch between the points of (1) the canines, (2) the mesio-lingual cusps of the first deciduous molars, (3) the mesio-lingual cusps of the second deciduous molars; on the lower arch between (1) the embrasures of the canine and first deciduous molar at the contact point, (2) the distal fossae of the first deciduous molars, (3) the central fossae of the second deciduous molars.

Data from these measurements of the dental arches are summarized in Table V and in Figures 7 and 8, comparison being made in the latter with the mean widths compiled by Lewis and Lehman[10] from a study of 170 children at the Merrill-Palmer School.

Losses and Gains in Width of Dental Arches of the Dionne Quintuplets

A striking feature of the growth curves of the dental arches of the Dionne quintuplets is the fact that they show periodic losses in width followed by gains. When Lewis and Lehman[1] found a similar series of fluctuations in the curve of the mean widths they stated: "The only explanation we can offer at present is that these fluctuations are due either to the presence of some malocclusion cases or to the small number of cases in the group." A different point of view, however, has been taken by Brash,[1,3] Smyth and Young,[14] and Broadbent,[3] all of whose views are based on the newer conception of the development of the dental arch. According to former theories that portion of the arch occupied by the deciduous teeth merely became part of a wider arc and was increased in height by bone accretion on the *lower border*. On the contrary Brash and others have shown that the increase in height is on the *alveolar border*, and that the teeth are in continuous movement, giving "a picture in which everything is relative and nothing fixed." The decreases which take place in the width of the dental arch according to Broadbent[4] "illustrate very graphically the developmental trend and impress upon us the limitations encountered when one attempts to record developmental changes by just a measurement of dimensions, with the expectation that there should always be an increase in the size with the passage of time."

Losses in width of the dental arches of the Dionne quintuplets are summarized in Table VI. Since moulds of the teeth were taken only once a year, the period of loss in width is not shown as well for Emilie, Cecile and Marie, as for Yvonne and Annette. Half-yearly models would probably have caught all the fluctuations, such as are seen in the arches of Yvonne during her fifth year (Figure 7).

Relative Sizes of Maxillary and Mandibular Arches of the Dionne Quintuplets

When the widths of the dental arches of the Dionne quintuplets are plotted and compared with mean widths compiled by Lewis and Lehman[10] (Figure 7) it becomes evident that the mandibular arch in each of the five children is proportionately narrower than the maxillary one. And while the maxillary arches have overcome their handicap of small size (probably associated in part with a premature birth), the mandibles have failed to do so.

It is this variation from the mean

*We are indebted to Miss B. Bott for assistance in this work.

which constitutes the condition of malocclusion. Although the malocclusion in the case of the quintuplets would be observed more easily by a dentist or by a parent when the child was seven years of age, nevertheless the condition has existed from infancy, as is shown in the graphs, and can be definitely traced back through the deciduous dentition.

The averages of the several measurements of the dental arches of the quintuplets have been compared with both the mean widths and standard deviations in Figure 8. Here it is seen that the average maxillary width between the canines of the quintuplets at seven years is greater than the mean; the average width between the first deciduous molars at seven years has reached the mean; while that between the second deciduous molars is less than the mean, but is still within the standard deviation. All mandibular widths, on the other hand, fall short of the standard deviation. Thus the condition of malocclusion is redemonstrated and its presence again traced back to infancy.

Summary

1. An account is given of the dentitions of the Dionne quintuplets from two to seven years of age.

2. The succession of eruption of their permanent teeth is shown to follow a developmental pattern belonging to the malocclusion series, as described by Hellman.[9]

3. A method is outlined by which the developmental pattern of eruption of the permanent teeth of the quintuplets is shown to be inherited.

4. The succession of eruption of the deciduous dentitions of the quintuplets is outlined and discussed.

5. The late eruption and anomalies in form of the second deciduous molars are discussed.

6. A method is described by which the width of dental arches may be accurately measured.

7. The growth curves of the dental arches of the Dionne quintuplets show periodic losses followed by gains, a feature to be expected according to the newer conception of the development of the arch.

8. Relative sizes of the maxillary and mandibular arches of the Dionne quintuplets are compared with mean widths compiled by Lewis and Lehman.[18] It is shown that the mandibles of the quintuplets are relatively narrow as compared with the maxillae and hence results the malocclusion.

9. The condition of malocclusion in the Dionne quintuplets is traced back through their deciduous dentitions to infancy.

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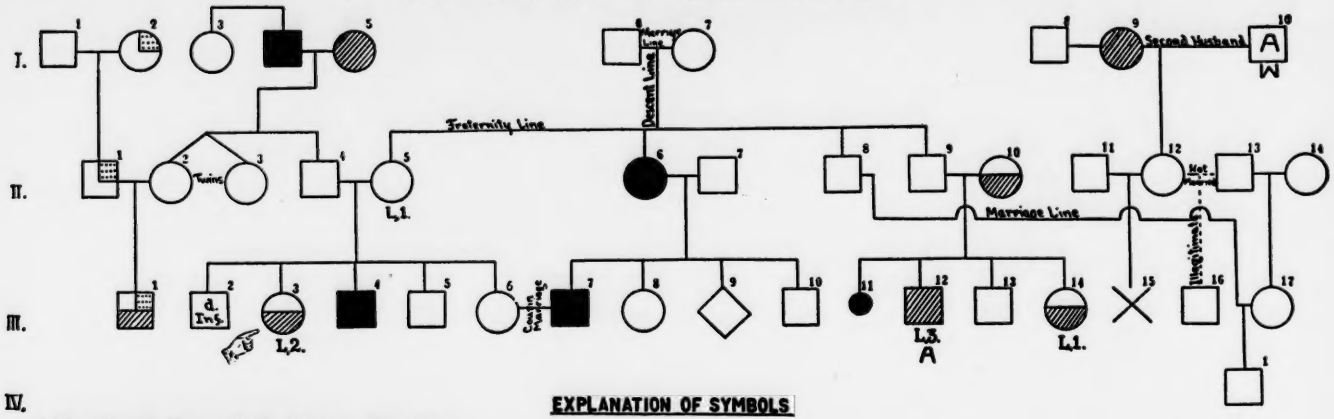

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□○=Parents.

□○□○○=Children.

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